1020 Ion Channel Variations and Drugs in the Genesis and Treatment of Arrhythmias

Sunday, March 06, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 10:00 a.m.-11:00 a.m.

1020-265 Common Human SCN5A Polymorphisms Have Altered Electrophysiology When Expressed in the Q1077 Splice Variants

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Background: The current through the Na channel encoded by *SCN5A* underlies cardiac excitability, and abnormalities in this current underlie various heritable arrhythmia syndromes. Recently, we reported the minor allelic frequencies of eight common (> 0.5%) polymorphisms in *SCN5A* detected in 4 major ethnic groups: R34C, R481W, S524Y, H558R, P1090L, S1103Y, R1193Q, and V1951L. Two splice variants of human SCN5A, one lacking a glutamine at position 1077 (Q1077del) and one containing Q1077, exist in every human. We engineered the eight polymorphisms in the two SCN5A splice variants to study their function.
Methods: We generated the point mutation by site directed mutagenesis in both variants and expressed them into HEK-293 cells for voltage clamp studies.
Results: 24 hr after transfection, only R34C and V1951L showed no functional differences in the two splice variants. First, we confirmed our earlier observation that current density for H558R is dramatically reduced when expressed in the Q1077 variant (-14±5 pA/pF n=8); similarly, S524Y in the Q1077 variant had significantly reduced current (-75±11 pA/pF n=28) compared to WT-Q1077 (-326±44 pA/pF n=21) p<0.0001. However, S524Y expressed in the Q1077del variant had current density similar to WT-Q1077 (-284±59 pA/pF n=20 for S524Y and -338±68 n=14 for WT-Q1077). Second, we found that the two variants have subtle but significantly kinetic changes for some of the polymorphisms. The Q1077del variant changed the mid-point of activation (SSA) in P1090L by -5 mV, in S1103Y by -3 mV. The Q1077 variant changed the SSA in S524Y by +3 mV, in H558R by +14 mV, in S1103Y by +5, and in R1193Q by -6 mV. The steady state of inactivation (SSI) was significantly left shifted for R481W (-6 mV) in Q1077del, and for R1193Q (-5 mV) in Q1077. Q1077 also shifted the SSI to the positive direction for S524Y, H558R, and S1103Y (by +3 mV, +10 mV, and +6 mV, respectively).
Conclusions: We conclude that many common SCN5A polymorphisms affect function to the same extent as that described for arrhythmia mutations such as Brugada syndrome and that the splice variant background used to study mutations is important. These findings have implications for the significance of clinical arrhythmia phenotypes.

1020-267A The Influence of Extracellular Acidosis on the Effect of Type III Antiarrhythmic Agents on the Cardiac Potassium Channel (IKr)

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Ischemia may cause major changes in pH. The change in pH could influence the effect of type III agents on the rapid delayed rectifier potassium channel (IKr). We evaluated the effects of acidosis on IKr inhibition caused by amiodarone (AM), azimilide (AZ), dofetilide (D) and quinidine (Q). IKr was studied at room temperature by using HERG gene expressed in Xenopus oocytes and two electrodes voltage clamp technique was applied. The recording bath solution contained in mmol/L: 96 NaCl, 5.0 KCl, 2.0 $CaCl_2$, 1.0 $MgCl_2$, 5 HEPES; and pH adjusted with NaOH to 6.2 or 7.4. AZ, AM, Q at 1, 3, 10, 30, 100 μM and D at 0.03, 0.1, 0.3, 1, 3 μM caused dose dependent block in HERG current. The IC_{50} was 5.8 ± 0.3 μM for AZ, 9.9 ±1.01 μM for Q and 0.5 ± 0.02 μM for D. When extracellular pH was decreased from 7.4 to 6.2, the IC_{50} increased to 96 ± 11 μM for AZ, 203 ± 16 μM for Q and 13 ± 1 μM for D. The block effect was decreased 32% for AZ, 42% for D, 29% for Q when pH was decreased from 7.4 to 6.2. For AM, the IC_{50} was 38 ± 9 μM at pH 7.4 and 27 ± 2 μM at and pH 6.2. There was no significant difference in the percentage of current block by AM between pH 6.2 and 7.4. Our data shows that the Ikr blocking effect of AZ, D and Q was attenuated at acidic pH while this was not the case for AM. The effect of AZ, D and Q at low pH creates heterogeneity of repolarization between ischemic and normal regions, but no change in current block would be expected with AM with regional acidosis. These observations may explain the reduced proarrhythmic effect of AM.

1020-267 Reentry Mediated by Ca^{2+} Transient: Roles of Intracellular Ca^{2+} on Graded Propagation and Conduction Block

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Background: When given during the vulnerable period, a single premature stimulus (S_2) of appropriate strength can induce reentry. A reentry pathway has been considered to be determined by the dispersion of refractoriness. Due to the complex interaction between transmembrane potential (Vm) and intracellular Ca^{2+} handling, we hypothesized that the intracellular Ca^{2+} transient (CaT) is associated with the formation of reentry.
Methods: A unipolar premature stimulation (S_2) with strong current (40-100 mA) was applied after 8 beats of baseline pacing (S_1) on the left ventricular epicardium in acquired with 4-ms/frame temporal resolution, using 2 charge-coupled device cameras. The fluorescence level was calibrated by S_1 induced AP, which we assumed to have a Vm varying between -90 mV to 10 mV and a CaT amplitude varying between 100 nM and 1000 nM.
Results: Cathodal and anodal S_2s initiated reentry. After reentering the S_2 site, Vm exhibited graded propagation. During the propagation in the reentrant pathway, the takeoff potential of Vm was significantly more depolarized at the entry site (cathodal S_2, -37±2 mV; anodal S_2, -38±5 mV) than at the exit site (cathodal S_2, -46±4 mV; anodal S_2, -49±7 mV). As activation propagated along the reentrant pathway, the amplitude of CaT significantly increased (cathodal S_2, 33±16 %; anodal S_2, 35±28 %). At the exit, the initial rise of CaT preceded that of Vm. When Vm was high enough to block the conduction near the S_2 site (cathodal S_2, -21±7 mV; anodal S_2, -22±2 mV), CaT near the S_2 site (cathodal S_2, 520±37 nM; anodal S_2, 542±48 nM) was greater as compared to when reentrant activation passed through (cathodal S_2, 412±51 nM; anodal S_2, 397±71 nM).
Conclusion: Reentrant propagation is mediated through the mechanism regarding elevated CaT increases intracellular cations. The propagation with elevated CaT at the exit suggests triggered activity. Further increase of CaT induces conduction block.

1020-268 Ranolazine Reverses the Changes in Cardiac Depolarization-Repolarization Patterns Caused by E-4031 and ATX-II. An Optical Mapping Study Using Experimental Models of LQT-2 and LQT-3 Syndromes

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Background: Ranolazine has clinical anti-anginal activity and is reported to suppress the arrhythmogenic effects of a number of QT-prolonging drugs in pre-clinical models.
Objectives: The purpose of this study was to determine the effects of ranolazine on dispersion of ventricular electrical activity in the absence and presence of either the late I_{Na}-enhancer ATX-II (LQT-3 syndrome model) or the I_{Kr}-blocker E-4031 (LQT-2 syndrome model).
Methods: Langendorff-perfused guinea pig isolated hearts were treated with ATX-II (3 to 20 nM), E-4031 (0.1 to 3 μM) or ranolazine (5 to 30 μM) alone and ranolazine combined with either ATX-II or E-4031. Action potentials were simultaneously recorded from 256 anterior right and left ventricular epicardial sites using a high-resolution photodiode-array-based optical mapping system. Action potential duration (APD) and ventricular transepicardial APD gradient (APD dispersion) were determined.
Results: Under control conditions, APD and transepicardial APD gradient were 179 ± 6 msec and 2.3 ± 0.3 msec/mm, respectively. ATX-II (20 nM; n=4) and E-4031 (3 μM; n=3) significantly increased the mean APD above control by 128% and by 58% respectively, and the APD gradient by 494% and 206%, respectively. Ranolazine alone (n=4) caused a 20% prolongation of APD (p<0.001) at the highest concentration (30 μM), but did not cause a significant change in the transepicardial APD gradient. Ranolazine, in a concentration-dependent manner, significantly (p<0.001 at 30 μM ranolazine) reduced the increases in APD caused by 10 nM ATX-II and by 1 μM E-4031 from 302 ± 18 to 224 ± 4 msec (n=8) from 261 ± 5 to 234 ± 4 msec (n=6), respectively. Ranolazine (30 μM) reversed the increase in the APD gradient caused by ATX-II from 6.1 ± 1.0 to 2.3 ± 0.2 msec/mm (p<0.01) and that caused by E-4032 from 3.9 ± 0.2 to 2.0 ± 0.1 msec/mm (p<0.001).
Conclusions: Ranolazine (30 μM) caused a moderate prolongation of the APD. However, ranolazine did not increase dispersion of APD as measured by the transepicardial APD gradient. On the contrary, ranolazine (30 μM) reversed the actions of ATX-II and E-4031 both to prolong APD and to increase the transepicardial APD gradient.

1020-269 Enhanced Cardiac L-Type Calcium Current Response to Urotensin II in Heart Failure

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Background. Urotensin II (U-II) is a somatostatin-like peptide recently identified as a potent vasoconstrictor with negative inotropic actions. In heart failure (HF) patients, circulating and myocardial U-II levels are increased, which suggest a pathophysiological role of this peptide. However, the cellular mechanism of U-II-induced cardiac depression is unclear. Virtually no previous studies have specifically examined U-II-induced changes in L-type Ca^{2+} current ($I_{Ca,L}$).
Methods. We assessed the effect of U-II on $I_{Ca,L}$ response in isolated left ventricular (LV) myocytes obtained from 16 rats with isoproterenol (ISO)-induced HF (4 months after 340 mg/kg, sq, for 2 days) and from 10 age-matched normal control rats. To examine the mechanism of U-II-induced changes in $I_{Ca,L}$, the U-II functional responses were also evaluated in 3 subgroups after the myocytes were pretreated with U-II receptor antagonist, Urantide (10^{-5} M), pertussis toxin (PTX, 2μg/ml, 36°C, 6h), and dibutyryl-cAMP (Db-cAMP, 10^{-4} M). $I_{Ca,L}$ was measured using whole-cell voltage clamp technique.
Results. Superfusion of U-II (10^{-8}-10^{-5} M) caused a dose-dependent decrease in $I_{Ca,L}$ in both normal and HF myocytes with maximal inhibition at 10^{-5} M. In normal myocytes, U-II (10^{-5} M) decreased $I_{Ca,L}$ by 14.3% (5.0±0.29 vs 5.9±0.3 pA/pF, p<0.01). In HF myocytes, the baseline $I_{Ca,L}$ was significantly lower (3.0±0.1 vs 5.9±0.3 pA/pF, p<0.01) and was further reduced by 31.3% with U-II 10^{-5} M (2.1±0.1 vs 3.0±0.1 pA/pF) that was significantly greater than U-II-induced changes in normal myocytes. U-II-induced reductions in $I_{Ca,L}$ were significantly attenuated by U-II-antagonist and were reversed after washout of U-II. In both groups of rats, U-II-induced decreases of $I_{Ca,L}$ were prevented with pretreatment myocytes with PTX (normal: 5.3±0.3 vs 5.3±0.2; HF: 3.0±0.3 vs 3.0±0.4 pA/pF) or Db-cAMP (normal: 5.2±0.2 vs 5.3±0.1; HF: 2.9±0.1 vs 2.9±0.3 pA/pF).
Conclusion. U-II inhibits L-type Ca^{2+} channel and decreases $I_{Ca,L}$ in both normal and HF myocytes. In HF, U-II-induced inhibition of $I_{Ca,L}$ was enhanced. These effects are likely to be mediated through cAMP-dependent mechanism and coupled with PTX-sensitive G-protein.

POSTER SESSION

1021 Atrial Fibrillation and Pharmacology

Sunday, March 06, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 10:00 a.m.-11:00 a.m.

1021-250 Angiotensin II Receptor Blocker Reduces Plasma B-type Natriuretic Peptide Level in Patients With Atrial Fibrillation: A Randomized, Open-Label, Controlled Study

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Background: Plasma B-type natriuretic peptide (BNP) is elevated in medically stable outpatients with chronic atrial fibrillation (AF). The purpose of this study was to assess plasma BNP level as a result of administration with angiotensin II receptor blocker (ARB), that has beneficial effects on AF, in pts with chronic nonvalvular AF.
Methods: This study was a single-center randomized, controlled, open-label study during two years (from April 2001 through December 2003), and seventy-six pts initially enrolled. Fifty-eight subjects (37 men, age 68±10 yrs) were included in the analysis. Of these, 28 were allocated to ARB group (losartan 50mg per day), and 30 to control group.
Results: In terms of base-line characteristics, ARB group and control group were well matched. 1) At baseline, BNP level was significantly greater in pts with chronic AF (n=58) than in normal subjects (n=89) (131.9±111.4 vs 25.2±31.1 pg/ml, p < 0.0001), however, did not differ between pts with ARB administration (ARB group, n=28) and pts without ARB (control group, n=30) (140.1±104.3 vs 124.3±118.9 pg/ml, p=0.5923). 2) During a mean follow-up period of 24±4 months, in ARB group, plasma BNP level was significantly decreased (140.1±104.3 to 114.7±92.6 pg/ml, p=0.0163; a 50.1 percent decrease), however, there was no significant change in control group (124.3±118.9 to 114.1±135.5 pg/ml, p=0.9294). In both group, there were no significant differences in hemodynamic performance including blood pressure or heart rate.
Conclusion: This is first report to show that angiotensin II receptor blocker reduces plasma BNP in pts with AF. This study suggests that the association of renin-angiotensin system with nonvalvular AF and may provide the rationale for clinical trials to investigate the use of ARB in the management of chronic AF.

1021-251 Propafenone-Sotalol: Which Is Preferred in Atrial Fibrillation, for the Maintenance of Normal Sinus Rhythm

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Background. In this prospective, randomized, single-blinded, placebo-controlled trial, we assessed and compared the efficacy and safety of sotalol and propafenone when used long-term for the prevention of atrial fibrillation. Previous studies with both agents have reported favorable clinical results but limited data are available on the long-term effectiveness of such drugs.
Methods. We studied 254 consecutive patients (128 men, mean age 63 ± 9 years) with recurrent, symptomatic atrial fibrillation. After restoration of sinus rhythm, patients were randomized to propafenone (450 mg/day), to sotalol (160-480 mg/day as tolerated) and to placebo. Follow up clinical evaluations were conducted at the 1st, 2nd, 4th and 6th month and at 3-month intervals thereafter. The proportion of pts remaining in sinus rhythm was calculated for the two groups using the Kaplan-Meier method. End point of the study was recurrence of atrial fibrillation or occurrence of side effects necessitating discontinuation of medication.
Results. Of the 254 patients, 86 were assigned to propafenone, 85 to sotalol and 83 to placebo. Of the 86 patients receiving propafenone 45 relapsed to atrial fibrillation and/or experienced intolerable side effects after a mean time of 26 months, compared to 69 of the 85 sotalol patients after a mean time of 18 months and 73 of 83 controls after a mean time of 11 months (p<0.001 for propafenone and sotalol vs. placebo; p<0.001 for propafenone vs. sotalol).
Conclusion. Both propafenone and sotalol can be used for the maintenance of sinus rhythm in patients with recurrent symptomatic atrial fibrillation. However, for long-term maintenance propafenone seems to be more effective than sotalol.

1021-252 Long-Term Outcome in Patients With Atrial Fibrillation Treated According to the Guidelines for Antithrombotic Therapy in Comparison to Patients in Whom Guidelines Were Not Implemented

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Aim of this single center observational study was to compare the outcome in patients (pts) with atrial fibrillation (AF) implementing antithrombotic treatment(ATT) according to the guidelines with pts not treated as recommended by the guidelines.
Method: In this prospective AF registry 750 pts were included with AF. Pts were defined according their individuell risk for thromboembolic complications (TEC) in high risk pts (defined if one of the following risk indicators (RI) was positive: age > 75 yrs, org. heart disease, prior embolism, > 1 intermediate RI); intermediate risk pts (defined as age 65 - 75 yrs, diabetes or hypertension) and low risk pts (age < 65 yrs, no RI). ATT was recommended according to the guidelines: high risk pts received oral anticoagulation (OAC), intermediate risk pts OAC or ASA, low risk pts no OAC.
At the end of follow-up with a median of 65 months (50-84 months) pts were classified as follows: group 1 ATT according to the guidelines vs group 2 ATT not implemented as recommended. Follow up was complete in 93 % of pts.
Conclusion: 1) Pts with atrial flutter were less often treated with OAC compared to pts with AF. 2) Pts treated as recommended by the guidelines had a better prognosis in respect of mortality/stroke/severe bleeding compared to pts without implementing the guidelines for ATT as recommended.

pts characteristics (*p<0.05)	Group 1 as recommended by guidelines (576 pts)	Group 2 ATT not implemented as recommended (174 pts)
atrial fibrillation	76%	49%*
atrial flutter	41%	73%*
org. heart disease	84%	74%
hypertension	63%	42%*
prior stroke	14%	8%*
long-term follow-up:		
death	26.4%	32.3%*
stroke	5.6%	8.3%*
bleeding	1.0%	1.8%

1021-253 Amiodarone or Carvedilol Pretreatment Improves Conversion Rates in Persistent Atrial Fibrillation Patients - Clinical and Electrophysiological Outcomes

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Background: Pre-treatment with antiarrhythmic agents could improve cardioversion and atrial fibrillation (AF) recurrence rates in patients with persistent AF. In this prospective trial we examined the conversion and recurrence rates of persistent AF patients pre-treated with the b-blocker carvedilol and amiodarone.
Methods: One hundred forty-five patients were randomly assigned to treatment with carvedilol, amiodarone or placebo for four weeks prior to electrical cardioversion for persistent AF. The mean fibrillatory cycle length interval (FF) was evaluated before cardioversion and effective refractory period (ERP) was measured five minutes after restoration of sinus rhythm. Holter recordings were obtained from all patients on the day after cardioversion and the density of supraventricular ectopic beats was calculated.
Results: Cardioversion rates were 43/47 (91.5%) for carvedilol, 42/45 (93.3%) for amiodarone and 33/45 (73%) for placebo, making both drugs statistically superior to placebo (p=0.017). Both drugs prolonged FF and ERP in the setting of atrial remodeling due to AF and this could be related to their beneficial effect on conversion rate. Total AF recurrence rates during the first month after conversion were 27.9%, 16.6% and 39.4%, for the three groups respectively. The superiority to placebo was statistically significant only for amiodarone. Amiodarone patients also had a significantly lower density of supraventricular ectopic beats post-conversion.
Conclusions: The combination of electrical cardioversion with amiodarone or carvedilol is more effective than cardioversion alone in persistent AF patients. Amiodarone is superior in terms of sinus rhythm maintenance post-conversion. This could be related to the lower density of supraventricular ectopic beats.

1021-254 Comparison of a Na^+ and K^+ Channel Blocker on Electrophysiological Properties of the Pulmonary Veins in Patients With Atrial Fibrillation

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Antiarrhythmic agents are used for the treatment of atrial fibrillation (AF). However, the effects of antiarrhythmic drugs on the electrophysiological properties of the pulmonary veins (PVs) have not been well characterized. Therefore, we assessed the effects of pilsicainide (PLS), a pure Na^+ channel blocker (class Ic drug), and nifekalant (NFK), a pure IKr blocker (class III drug), on the electrophysiological characteristics within the PV and at the PV-left atrial (LA) junction using multielectrode basket catheter.
Methods and Results: PV mapping using a basket catheter was performed in 22 patients (19 men; mean age 58 ± 12 years old) with paroxysmal AF. Thirty-two bipolar electrograms were recorded simultaneously from a basket catheter. Thirty-four PVs, including 12 left superior, 6 right superior and 4 left inferior PVs, were studied at 58 pacing sites. The proximal electrode of the basket catheter was located at the PV-LA junction. The programmed stimulation was performed in the distal PV and PV-LA junction before and after infusion of PLS (1 mg/kg) in 12 patients or NFK (0.3 mg/kg) in 10 patients. Both drugs significantly prolonged the effective refractory period (ERP) of both the distal PV (PLS; from 165±34 to 186±45 ms, P<0.02, NFK; from 197±43 to 211±50 ms, P<0.05) and the PV-LA junction (PLS; from 203±56 to 213±60 ms, P<0.05, NFK; from 232±36 to 264±39 ms, P<0.0001). The degree of ERP prolongation by PLS in the distal PV was significantly higher than that in the PV-LA junction (15±17 vs. 4±18 %, P<0.05), whereas that by NFK in the PV-LA junction was significantly higher than that in the distal PV (15±7 vs. 6±9 %, P<0.05). PLS significantly prolonged the conduction time (S_1-A_1) from the distal PV to PV-LA junction (from 45±16 to 60±19 ms, P<0.05), and in a patient with induced sustained AF, PLS blocked the conduction from the LA to PV at the PV-LA junction, and then terminated AF. In contrast, NFK did not change the conduction time in PVs.
Conclusions: In patients with AF, PLS has antiarrhythmic effects mainly on the distal PV by modifying the ERP and the conduction properties. In contrast, NFK has antiarrhyrhmic effects mainly on the PV-LA junction by modifying the ERP.

POSTER SESSION

1022 Ventricular Tachycardia: Potpourri

Sunday, March 06, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 10:00 a.m.-11:00 a.m.

1022-255 Clinical Value of Repeating Indeterminate Microvolt T-Wave Alternans Tests

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Background: Microvolt T-Wave Alternans (MTWA), a non-invasive test for assessing ventricular tachyarrhythmic risk, has had reported rates of indeterminate test results typically in the 20% to 30% range. The effect of repeating indeterminate MTWA tests on the overall indeterminacy rate is unknown.
Methods: The MASTER Trial is a 1500 patient prospective study evaluating MTWA as a predictor of future spontaneous ventricular tachyarrhythmic events in patients with prior myocardial infarction and LVEF ≤ 0.40. This trial uses the Heartwave™ (Cambridge Heart, Inc.) for measuring MTWA. The protocol requires that all tests classified by the automated report classifier as indeterminate be repeated at the same testing session as the initial test. Final classification of MTWA tests was determined by an expert reader blinded to the clinical data. An interim analysis of the effect of repeating indeterminate MTWA tests on the overall indeterminacy rate was performed.
Results: Of 606 initial MTWA tests, 113 (18.6%) were classified as indeterminate. The causes of indeterminacy were: non-sustained alternans (32.7%), bad beats (32.7%), inadequate heart rate (23.0%), noise (10.6%), and heart rate rise too rapid (0.9%). Repeat testing was performed on 65 of these patients and resulted in a determinate result in 60%of the repeated tests (MTWA positive in 35.4%, negative in 24.6%, indeterminate in 38.5%, and technically inadequate in 1.5%). The initial cause for indeterminacy was not significantly associated with whether repeating the test would yield a determinate result. Final classifications for 606 patients included 280 (46.2%) as Positive, 240 (39.6%) as Negative, 59 (9.7%) as Indeterminate, and 27 (4.5%) as Technically Inadequate.
Conclusion: Repeating MTWA tests initially classified by the automatic report classifier as indeterminate results in a determinate result in 60% of repeated tests and reduces the overall indeterminacy rate to 9.7% (margin of error 2.4%) which is substantially lower than previously reported.

1022-256 The Prognostic Value of Consecutive Abnormal Signal-Averaged Electrocardiograms in Patients after Acute Myocardial Infarction

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Objective: To assess the prognostic ability of consecutive abnormal signal-averaged electrocardiograms (SAECGs) during hospitalization after an acute myocaridal infarction (AMI).
Methods: Seven hundred and five pts (525 men), aged 63±0.4 (SE) years in sinus rhythm were studied prospectively post-AMI. All pts underwent 1) Estimation of functional Killip class on admission, 2) SAECG obtained at the 1st, 3rd and 7th days after admission. Abnormal SAECG was defined if fQRS>114 ms plus either LAS>38 ms or RMS<20 μV for a standard QRS duration <120 msec or fQRS>155 ms, LAS>55ms or RMS<17 μV for a QRS≥120 msec. 3) Measurement of ejection fraction (EF) by 2D-echo on 1st day. 4) 24-hour Holter ECG recording with arrhythmias analysis based on Lown's classifications. 5) 12-lead ECG estimation of infarct size by QRS score based on Q and R wave duration and R/S and R/Q ratio at hospital discharge. Thrombolysis was given in 58% of pts. A cohort of 60 pts had consecutive abnormal SAECGs.
Results: During a follow-up period of 39±0.9 months 178 (25%) pts died of cardiac causes (including sudden cardiac death). The presence of the 3 consecutive abnormal SAECGs was correlated with age (p=0.00), EF (p=0.00), old MI (p=0.05), anterior AMI (0.00), QRS score (0.00) and Killip class>II (p=0.00). In multivariate analysis (logistic regression) only age (p=0.001), EF (p=0.002) and abnormal consecutive SAECGs (p=0.00) were independent predictors of cardiac mortality. The presence of 3 consecutive abnormal SAECG had higher specificity and higher positive predictive value (96% and 65%) than the separate abnormal SAECG (89% and 52% for the 1st, 90% and 42% for the 3rd or 87% and 32% for the 7th day respectively).
Conclusion: The presence of consecutive abnormal SAECGs improved the independent prognostic value of the SAECG for cardial mortality.

1022-257 The Shortage of Short QTs

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Background: Ventricular tachyarrhythmias and syncope or sudden death has recently been associated with a short QT interval (QTc <300 msec, the so-called Short QT interval Syndrome, SQTS). We investigated the prevelance of short QT intervals and the frequency of SQTS when the QTc is <300 msec.
Methods and Results: QTc was measured by a Marquette MAC 5000 and verified by a cardiologist at 25 mm/sec paper speed. From 1988 to July 2004, 479,120 consecutive electrocardiograms (ECGs) were analyzed by the MAC 5000, which reported 215 tracings with QTc <300ms. Each of these 215 ECGs were then measured manually but no QTc <300 msec was validated: 67% were found to be in error because of a pacemaker spike, 17% had supraventricular tachycardia with inaccurate detection of T wave offset, as from flutter waves, and 16% were found to have an error in cycle length calculation. Therefore, not one of the 479,120 ECGs were found to have a QTc <300ms.
We surveyed QT intervals in 80 subjects (40 men) after exclusion of tracings with bundle branch block, heart rates >100 beats per minute (bpm), ST depression or T inversion consistent with ischemia, or left ventricular hypertrophy with QRS widening. Patients were excluded if taking drugs that might cause QT prolongation. Average QTc for men was 425 msec ± 20 SD and for women: 436 ± 19. Combining sexes, 95% confidence interval for QTc = 392-468 msec. QTc<300 msec then would be >5 SD less than mean QTc, presumably reflecting 1 of 100,000 of our hospitalized subjects.
There were 50 patients in sinus rhythm <100 bpm with a relatively short QTc (350-360 msec per the Marquette MAC 5000) were validated by manual measurement to insure that the device did not systematically overestimate QT interval measurements and thereby fail to detect some patients with a true QTc <300 msec. Indeed, the physician measurement tended to be longer (average 373 msec ±39) than the computer average (362±33, r = 0.83).
Conclusions: SQTS has received considerable attention over the past few years, but only cases from seven families have been reported. A review of our hospital database failed to reveal new cases of QTc <300msec, suggesting that SQTS is quite rare.

1022-258 Localization of Idiopathic Ventricular Tachycardia Originating in Basal Left Ventricle: Utility of Distinct Electrocardiographic Features

Sanjay Dixit, Edward Gerstenfeld, David Callans, David Lin, Henry Hsia, Hemal Nayak, Ralph Verdino, Joshua Cooper, Andrea Russo, Vickas Patel, Erica Zado, Francis Marchlinski, University of Pennsylvania Health System, Philadelphia, PA, Philadelphia VAMC, Philadelphia, PA

Background: Pace maps (PM) from various basal left ventricle (BLV) locations manifest unique ECG morphologies. In this study we test the accuracy of PM derived ECG criteria in predicting site of origin (SOO) of idiopathic ventricular tachycardia (IVT) arising from BLV.
Methods: From 1/99 to 12/03, 122 patients (pts) underwent IVT ablation at our center of which 14 had fascicular VT. In remaining 108 pts, successful ablation site on 3-D electroanatomic map was from: right ventricular outflow tract in 88, aortic cusps / LV epicardium in 9 and basal LV endocardium in 11. The latter group manifested 12 VTs, which were reviewed by a blinded investigator (BI) who predicted SOO using criteria outlined in table below. At least 3 of 4 criteria had to be met for predicting SOO.
Results: Average age of study population was 58±20 years (8 males; LV Ejection Fraction 0.54±0.8). Successful ablation site was as follows: septal-parahisian (S-P) - 2, aorto-mitral continuity (AMC) - 4, superior mitral annulus (MA) - 3 and supero-lateral MA - 3. BI was able to accurately localize SOO of IVT in 10 of 12 cases (83%). In 2 cases SOO was incorrectly identified as superior MA and S-P region (successful ablation site was AMC in both).
Conclusion: PM derived specific ECG features can be used to accurately localize IVT originating from BLV. This may facilitate intracardiac mapping and ablation of these arrhythmias.

* Reversal of Q to R and vice versa < V3 = Early and > V5 = Late

	S-P	AMC	Superior MA	Supero-Lateral MA	Lateral MA
Lead I	R or Rs	Rs or rs	rs or rS	rS or QS	rS or rs
Lead V_1	QS or Qr	qR	R or Rs	R or Rs	R or Rs
Precordial Transition*	Early	None	None	None	None or Late
Ratio of QRS in leads II and III	>1	≤1	≤1	≤1	>1

1022-259 Transesophageal Defibrillation: A Therapeutic Option For Refractory Ventricular Fibrillation?

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Objektive: Shock-resistant or recurrent ventricular fibrillation occurs in about 10-25% of out-of-hospital resuscitations. Because of the proximity of the electrodes to the heart transesophageal defibrillation might increase defibrillation success. The study evaluated the comparative efficacy of a device for transesophageal defibrillation to transthoracic defibrillation.
Methods: After induction of VF monophasic and biphasic shocks were delivered between 2 cutaneous electrodes or between transesophageal and cutaneous electrodes. To evaluate the optimum transesophageal electrode configuration defibrillation thresholds (DFTs) were measured in 12 pigs (68±4kg) for 4 different electrode configurations. Choosing the optimum configuration DFTs were determined for external and transesophageal defibrillation in 10 additional pigs with lower body weight (39±1kg).
Results: Lowest DFTs were achieved with 1 large esophageal electrode vs. 2 external electrode patches. In 5 of 12 pigs with high body weight external defibrillation failed with maximum energy (200 J biphasic, 360 J monophasic shocks) whereas transesophageal defibrillation was still successful. In the remaining 7 pigs, DFTs were significantly lower for transesophageal defibrillation than for transthoracic defibrillation (biphasic: 67±27 vs. 164±23 J, monophasic: 171±45 vs. 320±56, p<0.001). In 10 pigs with lower body weight DFTs for transesophageal defibrillation were also significantly lower than for transthoracic defibrillation. Biphasic shocks yielded signficantly lower DFTs than monophasic ones. Long-term esophageal damage was ruled out by macro- and microscopic examinations in 6 mongrel dogs.
Conclusions: In this animal model, non-responders to external biphasic defibrillation could successfully be defibrillated with a transesophageal electrode configuration. Overall, a 35-50% DFT reduction was obtained by transesophageal defibrillation. Transesophageal defibrillation might increase primary defibrillation success rate and provide an additional tool for terminating VF which is refractory to external defibrillation.

1022-260 Effects of n-3 Polyunsaturated Fatty Acids on Arrhythmic Pattern in Chronic Heart Failure Patients

Chiara Vaccarini, Diego Domenighini, Giuseppe Furgi, Filippo Mastropasqua, Giorgio Mazzuero, Maria Rosa Perotti, Simona Sarzi-Braga, Maria Teresa La Rovere, Fondazione "S. Maugeri", IRCCS, Istituto Scientifico di Montescano, Montescano (Pavia), Italy

Background: N-3 polyunsaturated fatty acids (n-3 PUFA) found in fish or their dietary supplementation are associated with a reduced risk of sudden cardiac death, and experimental data suggest antiarrhythmic properties. Premature Ventricular Contractions (PVCs) have been regarded as a marker of increased arrhythmic risk. Preliminary data suggest that n-3 PUFA intake reduces the number of PVCs.
We evaluated the effects of n-3 PUFA in patients with chronic heart failure, a group at high prevalence of PVCs.
Methods and Results: One-hundred sixty-seven patients with ischemic (71%) or idiopathic cardiomyopathy (age 60±10 yrs, NYHA cl II 88%, Ejection Fraction 32±6%, stable therapy within the previous 3 months) were randomised to a standard dose of 1 gr/day of n-3 PUFA (SEACOR, SPA, Italy) or placebo for 6 months. Patients underwent 24h-ECG monitoring and plasma determination of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). At entry the two groups did not differ in terms of systolic arterial pressure (SAP, 114±14 vs 114±15 mmHg), heart rate (HR, 67±9 vs 66±10 b/min), PVCs /24h (1555±3937 vs 1153±2910), EPA (0.72±0.37 vs 0.74±0.44) and DHA plasma levels (2.1±0.6 vs 2.1±0.8 %fatty acids). One-hundred forty-two patients concluded the study, with the same drop-out rate in the two groups. At 6 months, no differences were found in SAP (116±16 vs 115±15 mmHg) and HR (67±10 vs 66±10 b/min), while there was a significant reduction of 55% in the total number of PVCs in the treatment group and an increase in the placebo group (705±1147 vs 1953±5064, $p = 0.036$); the same happened for the number of couplets and non sustained ventricular tachycardia events. Plasma levels of EPA and DHA were increased in the treatment group, with no change occurring in the placebo group (EPA 1.72±0.66 vs 0.78±0.38 DHA 2.9±0.8 vs 2.1±0.9 %fatty acids, $p < 0.001$). During the study 3 deaths were recorded: one stroke in the treatment and two sudden deaths in the placebo group.
Conclusions: These data suggest that the antiarrhythmic effect of n-3 PUFA can determine a reduction of PVCs in a population at high risk of sudden death. The increase in cardiac electrical stability observed in these patients does not correlate with a bradycardic effect.

1022-261 Elevation of Aortic and Coronary Artery Nerve Growth Factor Following Acute Myocardial Infarction in Humans

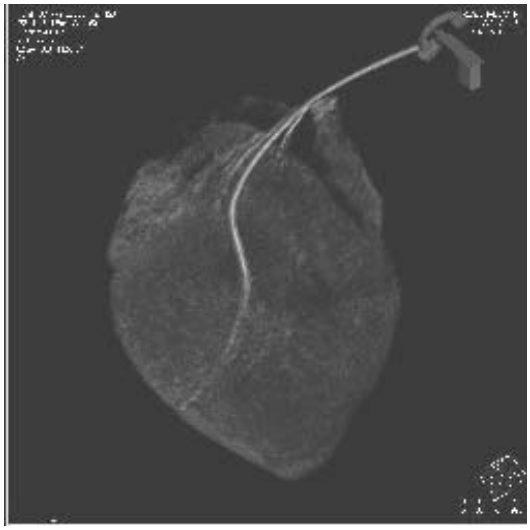
Saibal Kar, Simon Kangavari, Shengmei Zhou, Hongmei Li, Su-Chao Ding, Yii-Der Ida Chen, Lan S. Chen, Peng-Sheng Chen, Division of Cardiology, Cedars Sinai Medical Center and David Geffen School of Medicine of UCLA, Los Angeles, CA, Children's Hospital and Keck School of Medicine, USC, Los Angeles, CA

Background. We recently reported in a canine model that acute myocardial infarction (AMI) results in an upregulation of nerve growth factor (NGF) expression in the myocardium with peak activity at 1 week after MI. The total blood NGF rapidly increased after AMI, and stayed high for at least one month. The increased NGF was associated with cardiac nerve sprouting, which contributes to arrhythmogenesis after MI. We hypothesize that human patients with AMI might show similar increases in NGF levels with its resulting consequences.
Methods. Blood was drawn simultaneously from aorta and culprit coronary artery in ten AMI patients undergoing urgent cardiac catheterization. Serum NGF concentrations was quantified by using enzyme-linked immunosorbant assay. In each patient the time between blood sampling and the onset of chest discomfort was recorded
Results. There were 9 males and 1 female. The mean age was 63 yrs (range 42 to 82). There was no significant difference between the aortic and coronary arterial NGF levels in each patient. Patients with AMI > 6 hours had significantly higher aortic (235±131 ng/ml) and coronary artery (225±128 ng/ml) NGF levels than patients with AMI < 6 hours (58±71 ng/ml and 53±131 ng/ml, respectively, p=0.036 for both comparisons). The large standard deviation indicates a large individual variation of the NGF concentration. There is a good linear correlation between the time since the onset of chest pain and the NGF levels in the aorta (r=0.80, p=0.0057) and in the coronary artery (r=0.81, p=0.0048). One patient with a highly elevated NGF level (447 ng/ml) developed ventricular tachycardia nine months later, documented by an implantable cardioverter-defibrillator.
Conclusion. There is a time-dependent increase in systemic NGF concentrations in AMI patients. Increased NGF concentrations following AMI may cause increased cardiac nerve sprouting, resulting in an increases risk for serious ventricular arrhythmias.

1022-262 Use of Three Dimensional Image Rendering From Fluoroscopy to Determine Catheter Location in Excised Porcine Hearts

Amin Al-Ahmad, Michael Homer, Teri Moore, Paul J. Wang, Stanford University Medical Center, Stanford, CA

Background: Fluoroscopy has long been the standard for imaging of the heart during cardiac electrophysiological procedures. Catheter orientation within the cardiac chambers can often be difficult to precisely determine. New technology that renders a three dimensional (3-D) image from fluoroscopic imaging has become available.
Objectives: To validate the utility of 3-D image rendering from fluoroscopy in determining catheter position in excised hearts.
Methods: We placed a steerable catheter in 8 locations within 6 excised pig hearts. The heart was then placed under the fluoroscopy C-arm flat detector on a standard cath lab table. Using the AXIOM Artist dTA system (Siemens, Germany) a fluoroscopic scan was performed. A 3-D image was then rendered that could be manipulated on a computer screen and rotated in 360 degrees. The image contrast could be changed to see within the chamber to visualize the catheter, and see some surface landmarks. Using the scan, a blinded investigator was asked to precisely locate the catheter within the heart.
Results: The 3-D scan was successfully performed on all hearts in less than 30 sec. All images could be rotated to see all aspect of the heart. The catheter orientation, course and contact point with the wall could be seen. Catheter location could be accuratly determined in 40 of 46 images (87%).
Conclusion: The 3-D fluoroscopic scan technology shows great future promise for use in real time to aid in catheter position for mapping and ablation.



POSTER SESSION

1023 Pathophysiologic and Pharmacologic Modulation of the Electrocardiogram

Sunday, March 06, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 10:00 a.m.-11:00 a.m.

1023-247 Can Oral Magnesium Reduce the QTc Interval of Patients Receiving Class III Antiarrhythmics?

Brian F. McBride, Jeffrey Kluger, Bokyung Min, Danette Guertin, Craig I. Coleman, Burton Silver, Michael White, Hartford Hospital, Hartford, CT, University of Connecticut, Storrs, CT

Background: Intravenous magnesium (Mg^{++}) reduces the QTc interval of patients receiving ibutilide. This study was undertaken to evaluate the impact of oral Mg^{++} on the QTc interval of patients taking sotalol and dofetile and whether an inherent intracellular magnesium deficiency exists among patients with arrhythmias.
Methods: Patients (n=30) receiving sotalol or dofetilide for atrial or ventricular arrhythmias were randomized to receive twice daily Mg^{++} L-lactate (Niche Pharmaceuticals, 504mg elemental Mg^{++} daily) or placebo for 48 hours. A 12-lead ECG was taken at baseline, 3 hours, and 51 hours after dosing initiation to correspond to the Tmax after oral ingestion. The QTc interval was measured from the ECGs and compared between groups. Intracellular Mg^{++} concentrations were determined by energy-dispersive X-ray Analysis at baseline and 51 hours after dosing (Intracellular Diagnostics, Inc.; Foster City, CA).
Results: QTc interval reductions from baseline were greater in the Mg^{++} group than placebo (Table). Overall 63.2% of patients had baseline intracellular Mg^{++} concentrations below the normal reference range of 33.9-41.9mEq/IU with an average level of 32.6±2.2 mEq/IU. After Mg^{++} supplementation the intracellular concentrations rose significantly (36.2±2.4 mEq/IU, p=0.002) with all patients achieving normal concentrations.
Conclusion: Oral magnesium L-lactate raises intracellular magnesium concentrations and lowers the QTc interval of patients receiving sotalol or dofetilide.

QTc Interval	Magnesium (n=14)	Placebo (n=16)	P-value
Baseline	472.5±54	459.6±44	0.667
3 hours	435.9±64	450.4±48	0.015
51 hours	449.4±52	463.1±48	<0.001

1023-248 Clinical and ECG Covariates of QT/RR Slope in Congestive Heart Failure Patients

Iwona Cygankiewicz, Wojciech Zareba, Juan Manuel Cino, Jose Ramon Juanatey, Vicente Nieto, Alfredo Bardaji, Carlos Macaya, Jordi Fabregat, Antoni Bayes de Luna, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, Red Tematica Muerte Subita en el Adulto, Spain

Background: The aim of this study was to evaluate the relationship between QT/RR slope and clinical covariates and other ECG measures of risk in congestive heart failure (CHF) patients.

Methods. In the population of 454 CHF patients (NYHA class II or III), we evaluated the slope of the QTa/RR (QT apex) and QTe/RR (QTend) during 24-hour Holter recording (ELA Medical) and separately during day and night periods. The results of this analysis were correlated with clinical covariates (age, EF, etiology of disease, NYHA class), ECG variables (QRS, QTc) and heart rate variability parameters from Holter recording. **Results**.**1)** The mean± sd for QTe/RR was 0.19 ± 0.07 and for QTa/RR was 0.17± 0.06 and since they showed similar behavior we report results for QTe.
2) Association of QT/RR with clinical data: QT/RR slope showed significant negative association with ejection fraction (r=-0.18; p<0.01), i.e. lower ejection fraction was associated with steeper slope. Patients with idiopathic cardiomyopathy had steeper QT/RR slope than those with ischemic cardiomyopathy (0.20 vs. 0.18; p=0.03). There was no significant association between QT/RR slope and age and NYHA class.
3) Association of QT/RR with ECG data There was no correlation between QT/RR slope and QRS duration. QT-RR slope correlated significantly with QTc duration; i.e. patients with longer QTc had steeper slope (r=0.36; p<0.001). The QT/RR slope showed significant positive association with heart rate (r=0.40; p<0.001). There was significant negative association with several HRV parameters: SDNN (r=-0.31; p<0.001), SDNNI (-0.27; p<0.001), low frequency power (r=-0.32; p<0.001). The multivariate analysis adjusting for age and EF showed that increased QT-RR slope (above fourth quartile) is associated with increased heart rate and decreased heart rate variability. **3) Circadian variation of QT/RR**: The slope of QT/RR was significantly steeper during day vs. night hours (0.18 vs 0.17; p=0.001)
Conclusions: The QT-RR slope is dependent on ejection fraction, heart rate, and heart rate variability in CHF patients. This association indicates that prognostic value of QT-RR slope need to be evaluated while adjusting for these factors in respective subgroups.

1023-249 The Relationship Between Left Ventricular Geometry and Transmural Dispersion of Repolarization

Magdi M. Saba, Salman A. Arain, Salma S. Ibrahim, Jason A. Mitchell, Carl J. Lavie, Richard V. Milani, Ochsner Clinic Foundation, New Orleans, LA, University of Maryland, College Park, MD

Background: Previously shown, ventricular ectopic activity (VEA) is increased in patients (pts) with LVH but diminished in pts with concentric remodeling (CR), compared to normal cardiac structure. Increased transmural dispersion of repolarization (TDR), which correlates to the interval from the peak to the end of the T-wave (Tpe) on ECG, is linked to ventricular tachyarrhythmias. We describe the relationship between LV geometry and TDR.
Methods: Tpe was assessed by ECG in 400 pts (59% male) with normal LV systolic function, QRS < 120 ms, in sinus rhythm, divided into 4 equal, age- and sex-matched groups by echocardiographically determined LV geometry. LVH was defined as LV mass index (LVMI) ≥ 125 gm/m^2 , and relative wall thickness (RWT) was defined as 2 x posterior wall thickness/LV end-diastolic dimension, and was increased if > 0.43. Pts were divided into normal structure (no LVH, normal RWT), CR (no LVH, increased RWT), eccentric LVH (LVH, normal RWT) and concentric hypertrophy (LVH, increased RWT). Tpe interval was defined as the mean of 3 cycles from the precordial leads V1-V3.
Results: See table.

	Normal Structure (n = 100)	Concentric Remodeling (n = 100)	Eccentric Hypertrophy (n = 100)	Concentric Hypertrophy (n = 100)	ANOVA p-value
Age, yrs.	54.5 ± 3.0	54.8 ± 3.0	55.2 ± 3.6	54.9 ± 3.0	NS
BMI, kg/m^2	29.0 ± 7.9	32.8 ± 7.3[1]	31.7 ± 7.1[1]	31.9 ± 7.2[1]	0.0028
EF, %	61 ± 5	63 ± 3	62 ± 3	62 ± 6	NS
LVMI, gm/m^2	76.1 ± 17	76.8 ± 20	156.7 ± 14[1,2]	158.5 ± 38[1,2]	<0.0001
RWT	0.37 ± 0.04	0.51 ± 0.08[1]	0.39 ± 0.04	0.69 ± 0.8[1,2,3]	<0.0001
QRS, ms	89.3 ± 9.4	87.1 ± 11.2	94.1 ± 8.4[1,2]	98.6 ± 17.9[1,2,3]	<0.0001
QTc, ms	418.7 ± 20.7	416.1 ±19.5	425.9 ± 22.3[1,2]	441.3 ± 30.0[1,2,3]	<0.0001
Tpe, ms	88.6 ± 15.9	79.1 ± 13.6[1,3,4]	98.5 ± 10.2[1,2]	103.9 ± 25.8[1,2]	<0.0001
Tpe/QTc	0.20 ± 0.06	0.19 ± 0.03	0.23 ± 0.03[1,2]	0.24 ± 0.06[1,2]	<0.0001

[1,2,3,4] significantly different compared to respective column

Conclusion: Concordant with our previous observations of VEA and cardiac structure, TDR was increased in LVH but reduced in CR compared to normal structure. While LVH represents a maladaptive process resulting in an unfavorable electrical substrate, CR may represent a positive structural adaptation rendering a more favorable electrical milieu.

1023-270 Changes in QRS Amplitudes During Transient Right Bundle Branch Block: Effect on Voltage Criteria Used for the Detection of Left Ventricular Hypertrophy

Peter G. Chan, Michael A. Logue, Paul Kligfield, Weill Medical College of Cornell University, New York, NY

Background: Although right bundle branch block (RBBB) delays right ventricular depolarization, its theoretical "unmasking" of left ventricular forces by reduced cancellation in the early and mid-QRS might be offset or altered by directional changes in septal and right ventricular depolarization. Systematic changes in QRS amplitude during transient RBBB bear directly on performance of standard ECG criteria for left ventricular hypertrophy (LVH), and these changes require quantification during constant temporal and physiological conditions.
Methods: We examined the instantaneous effect of RBBB on QRS amplitudes and LVH voltages in 40 patients who had intermittent complete RBBB during a single 10 sec standard 12-lead ECG recording, comprising 0.01% of approximately 400,000 consecutive ECGs in a university teaching hospital setting. Amplitudes were measured by magnifying graticule to the nearest 25 microvolts, averaged for up to 3 normal and 3 RBBB complexes, and compared by paired t-test.
Results: RBBB was associated with an increase in mean initial rightward and inferior QRS forces (RV1, QV6, QIII) but significant decreases in mean leftward and posterior mid-QRS amplitudes that result from left ventricular depolarization (RaVL [-75 microvolts], SV1 [-389 microvolts], SV3 [-617 microvolts], RV5 [-100 microvolts], RV6 [-123 microvolts]). Mean late rightward and anterior QRS forces were increased with RBBB (R'V1, SV5, SI). As a result, combined voltages used for LVH criteria were significantly reduced by RBBB: Sokolow-Lyon voltage decreased from 1520 ± 739 to 1014 ± 512 microvolts (p<0.001), and Cornell voltage decreased from 1438 ± 683 to 746 ± 399 microvolts (p<0.001).
Conclusion: RBBB is associated with significant reduction in "left ventricular" QRS amplitudes of the standard ECG, suggesting cancellation, rather than unmasking, of mid-QRS forces by altered septal and delayed right ventricular depolarization. Because QRS voltages that are routinely combined for the detection of LVH are reduced in RBBB, standard LVH criteria will perform with lower sensitivity in patients with RBBB.

1023-271 A Novel Diagnostic Technique in Identifying Patients at Risk in Brugada Syndrome

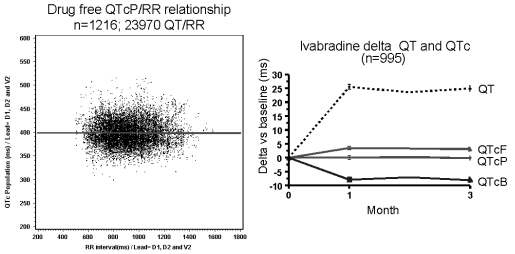
Takanori Ikeda, Satoru Yusu, Kentaro Nakamura, Masayuki Yotsukura, Hideaki Yoshino, Kyorin University School of Medicine, Tokyo, Japan

Background: The autonomic modulation, particularly high vagal tone plays an important role in the occurrence of ventricular tachyarrhythmias in Brugada syndrome. The full food intake is one of the factors of the modulation of vagal activity. We assessed clinical usefulness of a novel diagnostic technique, namely, a full stomach test in identifying high-risk group in Brugada syndrome.
Methods: We investigated changes of 12-lead electrocardiograms (ECGs) between before and within 30 minutes after a full meal in 37 patients (34 men; age 51 ± 15 years) with an ECG diagnostic of Brugada syndrome. We also analyzed several noninvasive markers such as late potentials by signal-averaged ECG, microvolt T-wave alternans, a mean QRS duration >120 msec, maximal QT interval >440 msec, and QT dispersion >50 msec. These values were compared to those of 30 control subjects who were matched for age and gender. A full stomach test was defined as positive when the augmentation of characteristic ECG abnormalities (i.e., a prominent coved-type ST-segment elevation ≥0.2 mV in leads V_1-V_2 at its peak) was seen after the meal.
Results: Life-threatening arrhythmic events defined as aborted sudden death or ventricular fibrillation were present in 12 (32%) of the 37 patients with Brugada-type ECG. The full stomach test was positive in 18 patients (49%) with Brugada-type ECG and none of the control subjects. The positive outcomes of the test were characterized by a higher incidence (56%) of life-threatening events than that (11%) in the negative outcomes (*P*=0.008), whereas there was no difference in signal-averaged ECG, microvolt T-wave alternans, a mean QRS duration, maximal QT interval, and QT dispersion. Multivariate logistic regression analysis revealed that the full stomach test had the most significant correlation to life-threatening events (*P*=0.015).
Conclusions: Characteristic ECG abnormalities augmented by a full meal is associated with the arrhythmogenesis of Brugada syndrome. The full stomach test could be a useful diagnostic technique for risk stratification in patients with Brugada-type ECG.

1023-272 Absence of Direct Effects of the If Current Blocker Ivabradine on Ventricular Repolarization: Analysis Based on a Population Heart Rate Correction Formula

Irina Savelieva, John Camm, St George's Hospital Medical School, London, United Kingdom

A selective If inhibitor ivabradine (IVA) has previously demonstrated anti-ischemic efficacy in a placebo-controlled trial and in a direct parallel comparison with atenolol. Prolongation of the uncorrected QT interval was observed with IVA as a result of its specific bradycardic action. Because of the inverse and non-linear relationship between the heart rate (HR) and the QT interval, conventional Bazett (QTcB) and Fridericia (QTcF) formulae for rate correction tend to under- or overestimate, respectively, the QTc interval. The aim of the study was to assess whether QT prolongation observed with IVA relates to bradycardia or a direct effect of IVA on ventricular repolarization. A population correction formula (QTcP) was developed and validated in a total of 23997 paired QT/RR values from the ECG recordings in 1216 matched drug-free participants in the Ivabradine Programme in coronary artery disease. (Figure, left). As determined by the analysis of the drug-free QT/RR values, the QTcP formula fell between the QTcB and QTcF formulae and was found to be truly independent of HR. The QTcP correction formula was then applied to 995 pts treated with IVA 10 mg bid for 3 months. Prolongation of the uncorrected QT interval was consistent with a decrease in HR but there were no changes in the corrected QTcP interval throughout the follow-up period (Figure, right). The QTcP correction formula provides evidence of the absence of any significant direct effects of IVA on the duration of ventricular repolarization.



1023-272A **Validation of RR-Irregularity Algorithm for Automatic Detection of Atrial Fibrillation on the Surface ECG**

Trang Dinh, Richard PM Houben, Vincent CMH Larik, Tim DJ Jongen, Michel HG Janssen, Harry JGM Crijns, Robert G. Tieleman, University Hospital Maastricht, Maastricht, The Netherlands, Medtronic Bakken Research Center BV, Maastricht, The Netherlands

Background: In atrial fibrillation (AF) it has been shown that more than half of the AF episodes are asymptomatic. Symptoms have a low discriminative power concerning presence of AF. Holter monitoring is labour-intensive, and has a low diagnostic yield. New automatic diagnostic tools are required for improvement of AF detection and determination of AF burden.
Methods: In cooperation with Medtronic Bakken Research Center BV an external loop-recorder with built-in analysis for AF detection was developed (AF alarm). Detection of AF was based on an algorithm evaluating RR-irregularity during 2-minute intervals. An exact copy of the AF alarm R-wave detection and rhythm analysis was implemented in Matlab® (The Math Works Inc.). This was used to analyze files from 2 datasets. Dataset 1 consisted of 24 ECG rhythm files from the Massachusetts Institute of Technology AF database. The 2nd dataset consisted of annotated 24-hour 3-lead Holter recordings (Marquette® MARS system) from 47 patients referred for evaluation of presence of AF.
Results: In dataset 1, 7,022 2-minute rhythm episodes were analysed. The AF alarm correctly identified 2,535 AF episodes (true positive, TP), and 3,865 non-AF episodes (true negative, TN). The AF-alarm wrongfully detected 359 false positive (FP) episodes. 273 AF episodes were not identified by the AF alarm (false negative, FN). In dataset 1, the sensitivity and specificity of the AF-alarm RR-detection and AF-analysis were 90.3% and 91.5%, respectively. The Holter recordings from dataset 2 were divided in 33,216 episodes of 2 minutes. 10,888 Episodes were annotated AF (TP). AF was absent in 21,269 rhythm episodes (TN). The AF-alarm wrongfully detected 383 FP episodes. In total 560 AF episodes were FN. In dataset 2, the sensitivity and specificity of the AF-alarm RR-detection and AF-analysis were 95.1% and 98.2%, respectively.
Conclusion: Using a custom-made algorithm based on RR-irregularity, AF can be reliably identified. Incorporation of this algorithm in an external ambulatory loop recorder with storage capacity for electrograms can improve diagnostic yield of AF detection, and especially the determination of AF burden.

POSTER SESSION

1050 Atrial Fibrillation and Flutter: Pathophysiology and Prognosis

Sunday, March 06, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 2:30 p.m.-3:30 p.m.

1050-247 **The Influence Of Ace Inhibitors On The Expression Of Bfgf And Vegf And The Microcapillary Density In Patients Whith Paroxysmal And Chronic Atrial Fibrillation**

Michaela E. Resetar, Heart Center Leipzig, Leipzig, Germany

Background: AF has been suggested to be associated with ischemic processes in a recent study. Therefore, we investigated the expression of angiogenic growth factors and microcapillary density in the atrium in patients with paroxysmal AF, chronic AF, non-ischemic patients in sinus rhythm (NISR) and ischemic patients in SR (ISR), additionally classifying groups with or without ACE inhibtor (ACE-I) treatment.
Methods: Atrial tissue samples were obtained from patients with lone AF (n=44) or sinus rhythm (n=17). Vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) protein levels were measured by quantitative Western Blotting techniques. Histological tissue samples were used for calculating microvessel density.
Results: The expression of bFGF in ISR, lone paroxysmal AF and lone chronic AF was significantly elevated versus NISR (p<0,001; p<0,05, p<0,01). The expression of VEGF exhibited similar results. The bFGF protein expression was systematically increased in patients in ISR versus lone chronic AF (p<0,05) and lone chronic AF versus lone paroxysmal AF (p<0,05).The microcapillary density was significantly decreased in paroxysmal AF (4,7cap./ 0,4mm2) and chronic AF (3,7cap.) versus ISR (6,3cap.) or NISR (7,7cap.). Lone chronic AF with ACE-I exhibited a significantly lower bFGF and VEGF protein expression compared to chronic AF without ACE-I (p<0,05). Interestingly, the microcapillary density was significantly higher in paroxysmal AF with ACE-I (p<0,01) and SR versus paroxysmal AF without ACE-I and chronic AF with or without ACE-I.
Conclusion: We speculate that lone AF is associated with a condition of ischaemia in humans, which might be positively influenced by ACE-I treatment.

1050-248 **Electrophysiological Mechanism of Atrial Fibrillation in a Novel Experimental Model of Left Atrial Volume Load**

Hiroya Ohmori, Takashi Nitta, Masami Ochi, Kazuo Shimizu, Nippon Medical School, Tokyo, Japan

Permanent AF is frequently associated with an LA volume loaded heart such as in mitral valve disease. However, the electrophysiological mechanism in this subset of AF has not been examined in an appropriate animal model. A novel experimental model that was highly relevant to human AF, consisting of an LA volume load achieved by a subclavian artery to pulmonary artery shunt and electrical remodeling induced by rapid LA pacing, was established and the electrophysiological consequences were examined in 10 canines. Rapid LA pacing was initiated at a paced cycle length of 100ms one week after the shunt surgery. Three animals died of severe heart failure in the early postoperative period. In the remaining animals, the LA diameter increased progressively from 27±4 mm preoperatively to 42±4 mm 5 weeks after the shunt surgery (p<0.05). The duration of the induced AF during a temporal suspension of the pacing prolonged progressively from 136±88 sec at the beginning of the pacing to a sustained AF (>10 min) within 4 weeks. The AF intervals measured at the LA appendages progressively shortened from 121±39 ms at the beginning of the pacing to 103±10 ms 3 weeks after pacing (p<0.05). The entire atrial epicardium was mapped with form fitted electrode patches with 246 bipolar electrodes and a three-dimensional dynamic mapping system during sustained AF 5 weeks postoperatively. The activation maps revealed repetitive activations arising from the pulmonary veins with fibrillatory conduction toward the RA in all animals and coexisting RA macroreentry in 3. Concurrent repetitive activations originated from the right and left superior pulmonary veins in 4 animals and a repetitive activation originated from the right superior pulmonary vein in 5, while no animals exhibited activations arising from the inferior pulmonary veins. The average cycle length of the repetitive activations originating from the pulmonary veins was significantly shorter than that from the RA. In conclusion, a volume load of the LA may provoke repetitive activations in the pulmonary veins, and electrical remodeling of the atrial myocardium further facilitates the perpetuation of AF.

1050-249 **Electrophysiologic Characteristics of Spontaneous Atrial Tachyarrhythmias in Patients with Refractory Atrial Fibrillation Defined by Combined Biatrial Catheter and Three Dimensional Noncontact Mapping**

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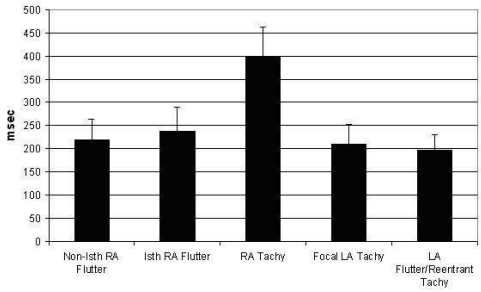
The electrophysiology of human atrial fibrillation (AF) in patients(pts) with heart disease, remains undefined.
Methods: We evaluated 59 pts with refractory AF, mean age 63 yrs, using combined biatrial catheter & 3 dimensional noncontact mapping (NCM). 47 pts had heart disease (Gp. 1) & 12 pts had no disease (Gp. 2).
Results: Sinus rhythm (SR, n=59), 104 atrial premature beats (APBs) in 51 pts (Gp. 1=40 pts {85%} & Gp. 2=11 pts {92%}) & 65 AF episodes in 41 pts were mapped. Mean P-wave duration in SR was 143 ms. Terminal atrial diastolic electrical activity was seen by NCM in selected pts in SR. APBs often arose in disparate RA & LA regions in the same pt. At AF onset, NCM demonstrated macroreentrant ATs in 46 pts (Gp.1 = 36, Gp.2 = 10) in RA or LA with a head to tail wavefront i.e.continuous electrical activation.Simultaneous ATs in RA & LA were observed only in Gp.1. Focal ATs were seen in 11 pts (Gp.1 = 8, Gp.2 = 3) & had centrifugal propagation with intermittent transatrial conduction. Focal ATs were more common in LA (9 pts) than RA (2 pts). LA flutter, focal LA AT & non-isthmus RA flutter had comparable rates (Figure) but were faster than RA ATs (p<0.04). Isthmus dependent RA flutter was slower than LA flutter (p<0.04) but faster than RA ATs (p<0.04).
Conclusions: 1. During human AF, macroreentrant ATs are more common than focal AT in pts with and without heart disease & occur with a biatrial distribution. 2. AT cycle lengths of LA focal ATs overlap with other ATs, & biatrial mapping with NCM is essential for accurate AT diagnosis.



1050-250 **Three-Dimensional Analysis of Left Atrial and Pulmonary Vein Anatomy: Implications for Balloon Catheter-based Circumferential Ostial Ablation**

Jameel Ahmed, Sandeep Sohal, Zachary J. Malchano, Jeremy N. Ruskin, Vivek Y. Reddy, Massachusetts General Hospital, Boston, MA, Boston Medical Center, Boston, MA

Background: Balloon catheters using various ablative energy sources are being developed to perform pulmonary vein (PV) isolation, but these must accommodate the variability in PV anatomy. Prior studies have examined PV anatomy using multi-planar 2D CT/MR images (long- and short-axis measurements). However, these studies may be limited by the frequent elliptical shape of the PV ostia, the non-orthogonal orientation of the PVs to the LA chamber, and difficulty in appreciating the frequency of common left PVs. To provide PV anatomical data relevant to the use of balloon ablation catheters, 3D surface reconstructions of LA-PVs were generated and analyzed to define ostial architecture and circumferential size.
Methods: Using MRI datasets obtained from 51 paroxysmal AF pts, the LA-PVs were segmented, and 3D surface reconstructions of the LA-PVs were generated and analyzed for ostial architecture using both external and endoluminal projections. The distance between the ostial border of the common left PV and the branching saddle-region separating the LSPV and LIPV was measured. PV circumferential measurements were made for each ostium.
Results: Left PVs: A common left-sided ostium was identified in all patients, with an ostial circumference of 95±14mm (range 70-129). Branching of the left PVs occurred 0-5 mm from the common left ostium in 23 pts (45%), 5-15 mm from the common os in 19 pts

(37%), and >15 mm from the common os in 9 pts (18%). In pts with a common os <15 mm (42 pts), the individual LSPV/LIPV ostial circumferences were 66±11mm (range 38-87) and 59±9mm (range 39-80), respectively. In pts with a common os >15 mm (9 pts), the ostial circumference was 88±9mm (range 73-99). Right PVs: The ostial circumferences of the RSPV/RIPV were 67±12mm (range 42-91) and 65±11mm (range 40-91), respectively. A distinct right-middle PV was observed in only 4 pts (8%), measuring 29±6mm (range 21-34). Based upon PV circumferences, the minimal diameter of a balloon ablation catheter required to isolate 95% of the RSPV, RIPV, LSPV, LIPV and LCPV are 29mm, 28mm, 28mm, 25mm, and 34mm.
Conclusion: Analysis of 3D surface reconstructions of LA-PV anatomy is invaluable to the design of balloon ablation catheters for PV isolation.

1050-251 Atypical and Typical Atrial Flutter Can Be Separated From the ECG Using Preferred Planes of Activation

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Background: Separating typical from atypical atrial flutter (AFL) from the ECG can be challenging, yet is central to guiding ablation. We hypothesized that typical AFL would show greater consistency in wavefront orientation than atypical AFL which is located less stereotypically.
Methods and Results: We studied 61 patients (51M, age 59.2±13.0), 39 with typical and 22 with atypical AFL (from location of concealed entrainment and successful ablation). For each, we generated a filtered atrial ECG from leads V5 (X-axis), aVF (Y) and V1 (Z) by correlating a 120 ms f-wave sample to successive ECG points. We generated loops of atrial cycles in the XY, YZ and XZ planes, and correlated successive loops as a measure of spatial *coherence* (range: 0-1). Three-dimensional spatial coherence (vector length) was greater for typical than atypical AFL (0.69±0.15 vs. 0.57±0.19; p<0.01). XY was the plane of greatest coherence for typical ($p<10^{-5}$ vs XZ or YZ) and atypical (p<0.015 vs XZ or YZ) AFL. However, the degree of coherence was greater for typical than atypical AFL in both XY (0.82±0.14 vs 0.66±0.24; p=0.002) and XZ (0.56±0.32 vs 0.35±0.39; p=0.03) planes. Notably, coherence in atypical right AFL was more evident in the XY plane, while coherence in atypical left AFL was more evident in other planes (atypicals: left vs right AFL: p<0.05).
Conclusions: Atypical AFL shows different preferred planes of activation than typical AFL on the ECG, likely reflecting anatomic and functional substrates. This ECG method may guide the approach to ablation, and provide mechanistic insights into AFL.

1050-252 The Degree of Diastolic Dysfunction Is Independently Associated With Atrial Fibrillation After Cardiac Surgery

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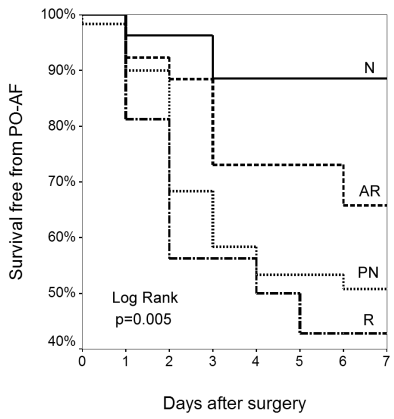
Background: Postoperative atrial fibrillation (PO-AF) is associated with increased morbidity and mortality. The relationship of preoperative diastolic function grade (DFG) with the risk for PO-AF has not been investigated.
Methods: 130 patients (mean age 61 ± 16 years; 33.1% women) in sinus rhythm undergoing any cardiac surgery other than mitral valve or for congenital abnormalities were prospectively enrolled. Preoperative DFG was categorized using Doppler echocardiography as normal (N), abnormal relaxation (AR), pseudonormal (PN), and restrictive (R). PO-AF was documented by continuous postoperative telemetry during the hospital stay.
Results: 50 (38.5%) patients developed AF after a mean of 2.7±2.4 days. Patients who developed PO-AF had a longer mean hospital stay (8.1 days, range 4-46) compared to those who did not (5.8 days, range 2-16; p<0.0001). Any diastolic dysfunction was associated with a higher risk for PO-AF [hazard ratio (HR)=4.52; 95% CI: 1.40 to 14.53; p=0.01]. A multivariate Cox model including DFG, age, history of atrial fibrillation, NYHA class and use of betablockers was built. Apart from age [HR=1.04; 95%CI: 1.02 to 1.06; p=0.001], DFG was the only independent predictor of PO-AF [HR=1.29; 95% CI: 1.05 to 1.59; p=0.01]. As shown in the figure, there was a graded positive association between DFG and the incidence of PO-AF.



Conclusion: DFG is strongly associated with the occurrence of PO-AF. Preoperative DFG is a superior means of stratifying the risk for PO-AF.

1050-267 Diabetes Mellitus Is a Strong Independent Risk for Atrial Fibrillation, Flutter, and Major Cardiovascular Disease

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Background: Diabetes mellitus (DM) is a major risk factor for coronary artery disease (CAD) and atherosclerosis. There is a controversy about correlation between DM and atrial fibrillation .The goal of this study was to evaluate DM as a risk factor for atrial fibrillation or flutter using a very large data base.
Method: We used PTF documents of inpatient treatment from all Veterans Health Administration (VHA) hospitals, extended care discharges and non-VHA hospital discharges at the Veterans Administration (VA) expense. The PTF contains demographic characteristics of patients and discharge diagnoses using ICD-9 codes. A total of 845,748 patients from this database were studied for the occurrence of atrial fibrillation and flutter. The cohort was stratified using DM (293,124) and a control group with hypertension (HTN) but no DM (552,624). Continuous variables were analyzed by unpaired t tests. Binary variables were analyzed using X2 tests and Fisher's Exact tests.
Results: Using univariant analysis, atrial fibrillations occurred in 43,674 (14.9%) DM patients vs. 57,077 (10.3 %) in control group (p<0.0001). Atrial flutter occurred in 11,852 (4%) DM patients vs. 13,554 (2.5%) of the control group (p< 0.0001). Using multi-variant analysis, DM remained a strong independed cause of atrial fibrillation with an odds ratio (OR) of 2.13, (95% Confidence interval (CI): 2.10 to 2.16; p<0. 0001) and flutter (OR 2.20 , CI: 2.15 to 2.26; p< 0.0001). Furthermore, congestive heart failure (CHF) (OR 3.12, CI: 3.09 to 3.16; p<0. 0001), LVH (OR 1.85, CI: 1.77 to 1.92; p<0. 0001) and CAD (OR 2.39 CI: 2.34 to 2.44; p<0. 0001) were also independently associated with DM.
Conclusion: This is the first large scale study finding DM as a strong, independent risk for the occurrence of atrial fibrillation and flutter. Furthermore, we confirmed the previous findings that DM is a strong predictor of LVH, CAD and CHF

1050-268 Gender Differences in Familial Atrial Fibrillation

Lin Y. Chen, Kathleen J. Herron, Curtis L. Olswold, Timothy M. Olson, Mayo Clinic, Rochester, MN

Introduction: Idiopathic or lone atrial fibrillation (LAF) may be familial in at least 15% of cases. We have observed a male predominance in patients with both sporadic and familial forms of LAF recruited for our genetic research studies. This may reflect referral or ascertainment biases, yet epidemiological studies also show LAF is 4-fold higher in males. To determine whether or not there is an intrinsic, gender-specific difference in disease susceptibility, we conducted a systematic study of familial LAF pedigrees.
Methods: Since November 2000, 135 unrelated patients referred to our Arrhythmia Clinic with LAF were enrolled into the study. LAF was defined as AF in patients < 60 years of age without hypertension or structural heart disease. Documentation of LAF was sought in relatives of patients with a positive family history for LAF. To eliminate potential gender-related referral bias, we excluded probands and compared males and females among affected relatives. Differences in proportions were tested using the Pearson Proportion Test. Differences in mean age at diagnosis were tested using the GENMOD (SAS version 8), a conservative test which accounts for potential biases introduced by analysis of unrelated pedigrees.
Results: A total of 65 probands with a family history of LAF (male=50, female=15) were identified. Of these, 24 probands had ≥ 2 relatives with documented LAF and inheritance consistent with autosomal dominant disease. When relatives only were analyzed (n=56), there was no difference between the proportion of males (52.5%) and females (47.5%) [p=ns]. However, there was a trend toward earlier age at diagnosis in males compared to females (mean age 45.2 vs. 52.4 yrs, p=0.07).
Conclusions: Both earlier age at onset and referral bias may account for the predominance of males with LAF observed in population and family based studies. Pedigree analyses suggest that male gender increases susceptibility to early-onset LAF.

1050-269 Atrial Fibrillation is an Independent Predictor for All-Cause Mortality in Ischemic Cardiomyopathy but not in Dilated Cardiomyopathy

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Aim of the study was to evaluate the prognostic impact of atrial fibrillation (AF) in ischemic cardiomyopathy (ICM) and dilated cardiomyopathy (DCM). **Patients and methods:** 1,119 unselected patients (P) with an ejection fraction (EF) ≤ 45% were prospectively and consecutively included into the LVD-registry Ludwigshafen (mean age: 67 years, 78% male, mean EF: 29%). Mean follow-up time was 27 months. All P received an optimized medical treatment for heart failure (93% ACE-inhibitor, 57% ß-blocker). AF or sinus rhythm (SR) was determined by standard ECG.
Results: P with ICM and AF (n = 112) were 5 years older (70 vs. 65 years, p<0.05) and had more often a reduced EF<30% (59 vs. 47%, p<0.05) than P with ICM and SR (n = 645). However, P with DCM showed no differences of age or EF when comparing the AF (n = 91) and SR group (n = 271). In a multiple logistic regression for all-cause mortality adjusted for 12 parameters (age, gender, diabetes, hypertension, COPD, prior stroke, EF, ACE-inhibitor, beta blocker, sotalol, amiodaron and oral anticoagulant), AF represented an independent prognostic factor in P with ICM, but not in P with DCM.

Multiple logistic regression for all-cause mortality

	ICM, OR (95% CI)	DCM, OR (95% CI)
AF	1.7 (1.2-2.6)	0.6 (0.3-1.0)
Diabetes	1.9 (1.4-2.8)	1.7 (0.9-3.0)
age >70 years	1.9 (1.4-2.7)	1.3 (0.6-3.0)
COPD	2.1 (1.4-3.2)	3.1 (1.8-5.6)
EF < 30%	2.7 (1.9-3.8)	3.4 (1.8-6.5)

Conclusion: 1. P with ICM and AF were 5 years older and had a lower EF than P with ICM and SR. In P with ICM AF represented an independent prognostic factor for all-cause mortality. 2. In P with DCM, however, there were no differences with respect to age or EF between the AF and SR group, and AF was not associated with a worse prognosis.

1050-270 5 Year Follow-up of Patients Presenting With First Episode of Atrial Arrhythmia: Comparison to Patients With Already Recurrent Episodes. A Single Center Experience

Torsten Becker, Klaus Dönges, Thomas Kleemann, Margit Vater, Ömer Yildiz, Karlheinz Seidl, Heartcenter Ludwigshafen, Ludwigshafen, Germany

Objective: Comparison of the long-term prognosis of patients (pts) presenting with the first episode of atrial arrhythmia versus those with recurrent episodes.
Methods: 1053 pts with atrial fibrillation or flutter were included in this single center registry and thereafter followed-up for 5 years regarding their long-term outcome and antithrombotic treatment (ATT) during this period.
Results: 618 pts (59%) presented with first episode of atrial arrhythmia vs. 435 pts (41%) with recurrent episodes. Baseline characteristics at index admission were as follows (first vs. recurrent): male 71% vs. 74% , median age 65 vs. 64 years, structural heart disease 58% vs. 59%, EF < 40% and NYHA II+ 13% vs. 8%. In 27% of pts with a first episode compared to 13% of pts with recurrent episodes ***(Odds ratio (OR) 2.4, CI 1.7-3.3)*** the arrhythmia triggered new diagnosis of structural heart disease. Long-term outcome and ATT during 5 year follow-up are shown in the table below:

	death	embolic events	severe bleeding	oral anticoagulation (OAC)	ASA
first episode	27%	5%	1.2%	58%	26%
recurrent episodes	16%	4%	0.9%	70%	15%
OR (CI)	***2.0 (1.4-2.7)***	1.4 (0.6-3.4)	1.4 (0.3-5.7)	***0.5 (0.4-0.7)***	1.4 (1.0-2.2)

Conclusions: 1. Mortality rate over a 5 year period was higher in pts with first episode of atrial arrhythmia than in those with recurrent episodes 2. This may be due to a higher proportion of pts receiving OAC in the group with recurrent episodes 3. Furthermore, compared to pts with recurrent episodes, a larger proportion of pts with first episode of atrial arrhythmia had previously undiagnosed and therefore untreated structural heart disease, suggesting atrial arrhythmias as a sentinel for structural heart disease and indicating poor prognosis.

1050-271 Rate And Prognostic Significance Of Atrial Fibrillation In Patients With Idiopathic Dilated Cardiomyopathy

Massimo Zecchin, Aneta Aleksova, Andrea Di Lenarda, Marco Merlo, Michele Moretti, Laura Massa, Gianfranco Sinagra, Struttura Complessa di Cardiologia, Trieste, Italy

Background: Atrial fibrillation (AF) is the most common sustained arrhythmia in patients (pts) with heart failure. Its incidence increases with aging and progression of heart failure. The prevalence of AF in pts with idiopathic dilated cardiomyopathy (IDC) is not known. Also its influence on the outcome of pts with IDC has never been extensively evaluated. The scopes of our study were to analyse the prevalence of AF and clinical characteristics of pts with AF at the baseline as well as the rate and prognostic significance of AF during long term follow-up in pts with IDC.
Methods: Data were obtained from 544 pts with IDC enrolled in the Heart Muscle Disease Registry of Trieste from 1978 to 2002.
Results: At baseline 512 pts (94%) had sinus rhythm, and 32 pts (6%) had AF (14 pts (2.6%) chronic and 18 pts (3.4%) paroxysmal AF). During the follow up of 81±58 months new onset of AF was observed in 50 pts (9.8%, 1.2/100 patient-years), 21 pts chronic (4.1%) and 29 pts paroxysmal (5.7%). Two, five and 10 years rate of chronic versus paroxysmal AF were 2.1% v 0.8%, 5.3% v 2.8% and 11.2% v 4.5% respectively. Pts with AF had more severe symptoms (NYHA III-IV 40% v 25%, p=0.02), lower end diastolic left ventricular diameter (35.62±5.2 v 37.91±7.28, p=0.03), were less frequently treated with beta blockers (38% v 56%, p=0.01) and were more on treatment with amiodarone (30% v 17%, p=0.03).
Two, five and 10 years rate of pts died or underwent heart transplantation (D/HTx) in sinus rhythm versus pts in AF were 11.5% v 20.4 %, 23.5 % v 39.3 % and 34.6% v 44.4% respectively, p=0.02. At Cox proportional model predictors for D/HTx were NYHA III-IV class (p<0.001), LV ejection fraction ≤0.30 + LV end diastolic diameter >70 mm (p<0.001), lower systolic blood pressure (p=0.014), presence of left bundle branch block (p=0.04). AF was not significantly related to the long term outcome (p=0.08).
Conclusion: The rate of AF in our group of pts with IDC was 15%. AF was more frequent among pts with more advanced disease, and also among those that were not receiving beta blockers. Its presence was not independent predictor of subsequent outcome.

1050-272 Lone Atrial Fibrillation in Olmsted County, Minnesota (1980-2000)

Yoko Miyasaka, Marion E. Barnes, Stephen S. Cha, Kent R. Bailey, James B. Seward, Walter P. Abhayaratna, Bernard J. Gersh, Teresa S.M Tsang, Mayo Clinic, Rochester, MN

Background: Lone atrial fibrillation (AF) is clinically defined as AF in the absence of structural heart disease. Using this definition, there are conflicting data with respect to prognosis and survival.
Methods: The complete medical records for residents of Olmsted County, MN, who had an ECG-confirmed diagnosis of first AF between 1980 and 2000 were comprehensively reviewed. We recorded every cardiovascular event and death in these patients without underlying structural heart disease, hypertension, diabetes mellitus, and had no reversible causes for AF. Survival of "lone AF" patients was compared with expected based on life tables for the Minnesota white population.
Results: A total of 4,618 residents were confirmed to have developed first AF between 1980-2000. Of these, 413 subjects (mean age 73.1± 14.4 years, 66% men) at the time of the first diagnosis of AF could be classified as lone AF, 120 (29%) of them died during a mean follow-up time of 8.3 ± 6.2 years. This represented a slight excess mortality (hazard ratio=1.2, p=0.051) compared to the general population of the same age, which was however confined to the patients who were 70 years or older (n=119, hazard ratio=1.25, p=0.04). Of 413 patients, 56 (13.6%) patients developed at least one documented cardiovascular event; including 6 (1.5%) with a transient ischemic attack, 5 (1.2%) with a stroke, 27 (6.5%) with congestive heart failure, 10 with ischemic heart disease (2.4%), and 16 (3.9%) with cardiovascular death.
Conclusions: Patients who developed first AF without any structural abnormality or additional cardiovascular risks represented a highly select minority of incident AF cases. As a group, they had a low cardiovascular event rate, and their survival appeared similar to that of the general population.

POSTER SESSION

1051 Optimizing Cardiac Resynchronization Therapy

Sunday, March 06, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 2:30 p.m.-3:30 p.m.

1051-253 Effects of Pacing Site on Left Ventricular Activation Sequences Using a Non-Contact Mapping System: Implications for Heart Failure Pacing

Dezhi Xing, Fausto G. Devecchi, Thomas R. Staley, David S. Glassman, James B. Martins, University of Iowa College of Medicine and VA Medical Center, Iowa City, IA

Background: Left ventricular pacing is effective in alleviating heart failure symptoms. The mechanisms of benefit and the optimal site of stimulation remain unclear. ***Methods*****:** To address these issues, bipolar pacing was undertaken in ten -chloralose open-chest dogs at ten sites, eight in the LV epicardium (EPI) and two in the RV including the interventricular septum. The cardiac activation of the entire LV was recorded with the EnSite 3000 (non-contact mapping) system and at twenty different endocardial (ENDO) locations using a steerable ablation catheter. Activation through the ventricular wall was also assessed transmurally with 23 multipolar plunge needles and ENDO pacing was performed using the endocardial-most electrodes. Virtual unipolar waveforms (non-contact mapping) generated from the array were compared with contact unipolars during sinus, EPI and ENDO pacing.
Results: Regardless of pacing site there was an excellent correlation between contact and virtual unipolars (non-contact). There was no significant difference in occurrence of a QS pattern (90-98% of the ENDO surface) between reconstructed electrograms during left ventricular EPI or ENDO pacing, irrespective of the pacing site. These findings correlated with the activation sequences recorded during sinus rhythm, in which endocardial to epicardial activation always occurs. RV (and septal) pacing showed an initial R wave in 90% to 100% of the reconstructed LV ENDO surface indicating that the Purkinje system was not at all involved with this activation.
Conclusions: Our data confirm that a more physiologic activation of the LV is achieved with any LV pacing site. This may reflect earlier engagement of the Purkinje network, which in turn more uniformly activates the rest of the ENDO surface compared with RV pacing activating predominantly via muscle. In our model, this activation pattern is irrespective from the LV pacing site chosen.

1051-254 Disparities Between Longitudinal and Circumferential Motion-Derived Analysis of Cardiac Dyssynchrony: Implications for Cardiac Resynchronization Assessment

Robert H. Helm, Christophe Leclerq, Owen Faris, Richard Tunin, Albert Lardo, David Kass, Johns Hopkins Medical Institution, Baltimore, MD

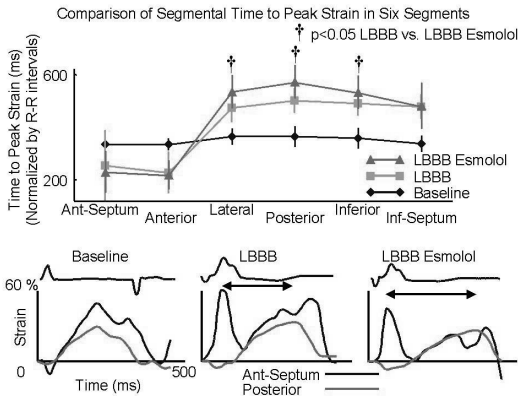
Background: QRS duration is widely used to identify cardiac resynchronization (CRT) patients, yet growing data supports the value of direct analysis of mechanical dyssynchrony. This is now commonly based on tissue-Doppler to measure longitudinal motion (ε_{ll}). However, contraction is principally circumferential (e.g. fiber direction, ε_{cc}), and whether dyssynchrony indexed by both orientations yields similar results is unknown.
Methods: ε_{ll} and ε_{cc} strain maps were generated from failing canine hearts with LBBB using tagged MRI. Dyssynchrony was assessed with two indexes: temporal uniformity (Leclercq, Circ, 2002;106:1760) and regional variance (Wyman, AJP 2002;282:372).
Results: ε_{cc} analysis showed that biventricular (BiV) and left ventricular (LVP) pacing improved synchrony in systole and diastole. In contrast, ε_{ll} analysis showed LVP improved synchrony during diastole only and BiV during both phases. It also had less sensitivity to synchrony overall (dynamic range of ε_{ll} indexes were ~50% of ε_{cc}). Despite differences in BiV and LVP with ε_{ll} -based analysis, both similarly improved global function (dP/dt_{max} and EF). (Table)
Conclusion: Dyssynchrony indexes derived from ε_{ll} have less sensitivity, follow different time courses, and may only manifest CRT benefits in specific cardiac phases depending on pacing mode. These data stress potential limitations to ε_{ll} -based dyssynchrony metrics, and support efforts to develop methods based on ε_{cc} to improve index performance and specificity.

	LBBB	LVP	BiV
dP/dt_{max}, mm Hg/s	1048 ±242	1309±339*	1392±413*
Ejection Fraction	23.0±12.7	28.0±16.1*	27.5±16.2*
Ecc-based DI in Systole	-18.0±4.2	7.0±3.0*	11.0±1.9*
Ecc-based DI in Diastole	-16.0±3.6	3.5±3.0*	12.3±1.9*
Ell-based DI in Systole	-3.1±1.5	-3.3±2.4	6.4±3.2*
Ell-based DI in Diastole	-6.9±1.4	0.1±1.3*	6.8±2.5*
* p< 0.05 verses LBBB baseline, DI = Temporal Uniformity Dyssynchrony Index (the more positive the index, the greater the synchrony)			

1051-255 **Deterioration of Left Ventricular Function Augments Regional Mechanical Dyssynchrony in a Model of Left Bundle Branch Block: Quantification by Angle-Corrected Radial Strain Imaging**

Kaoru Dohi, Michael R. Pinsky, Hideaki Kanzaki, Donald A. Severyn, John Gorcsan, III, University of Pittsburgh, Pittsburgh, PA

Background: The relationship of acute changes in contractility to mechanical left ventricular (LV) dyssynchrony is unknown. We tested the hypothesis that acute deterioration of LV function augments mechanical dyssynchrony, which can be quantified by strain imaging.
Methods: Ten open-chest dogs had angle-corrected subendocardial strain images from mid-LV short axis views (Aplio 80, Toshiba Corp). Pressure-volume loops were also recorded. Data were collected at baseline, right ventricular pacing to simulate left bundle branch block (LBBB), and during high-dose esmolol to induce heart failure. Dyssynchrony was defined as the time difference from earliest to latest peak strain among 6 radial sites. Heart rates were normalized.
Results: LBBB resulted in a large degree of dyssynchrony 346±64 ms* with early peak strain in the anterior wall 227±94 ms* and delays in the posterior wall 503±49 ms*, along with decreases in dp/dt -26±7 %*, and stroke work (SW) -59±18 %* (*p<0.05 vs. control). With esmolol, Ees decreased from 5.4±2.5 to 3.5±1.1* mmHg/ml (*p<0.05 vs. baseline). Esmolol-induced heart failure augmented dyssynchrony to 380±44 ms† with delays of posterior wall peak strain 563±61 ms† and further decreases in dp/dt -33±9 %† and SW -38±15 %† (†p<0.05 vs. baseline LBBB).
Conclusion: Angle-corrected subendocardial radial strain imaging demonstrated that LV dyssynchrony was augmented by acute deterioration in LV function in this model of LBBB and acute heart failure



1051-256 **Cardiac Resynchronization Improves Microcirculation**

Ayten Erol-Yilmaz, Bektas Atasever, Keshen Mathura, Jerome Lindeboom, Arthur Wilde, Can Ince, Raymond Tukkie, Academic Medical Center, Amsterdam, The Netherlands

Background: Although it is known that cardiac resynchronisation therapy (CRT) in heart failure patients improves systemic circulation, its acute effects on microcirculation are as yet unknown. To investigate this issue, we measured sub-lingual microcirculation changes in heart failure patients to CRT and right ventricular pacing by use of orthogonal polarization spectral (OPS) imaging.
Methods and Results: Twelve heart failure patients and 10 healthy controls were included. Six months of CRT resulted in decrease of NYHA classification and echocardiographic reverse remodeling. In these responders to CRT, acute microcirculatory changes were assessed by functional capillary density (FCD) and capillary velocity (CV). FCD and CV were measured sub-lingually after 15 minutes of programming in one of the pacing modalities (no pacing, right ventricular pacing, and biventricular pacing). FCD was significantly higher in healthy controls (10.9 ± 1.9, cm/cm2) compared to right ventricular pacing (8.9 ± 1.9, cm/cm2 , p=0.025) and no pacing (8.3 ± 2.4, cm/cm2, p=0.008). Biventricular pacing (12.1 ± 2.2, cm/cm2) significantly increased FCD compared to right ventricular pacing (8.9 ± 1.9 cm/cm2, p=0.03) and no pacing (8.3 ± 2.4, cm/cm2, p=0.018). CV was normal in all patients with or without pacing.
Conclusion: These study results showed for the first time that CRT directly improves microcirculatory function in CRT responders. Application of sublingual OPS imaging could be used to evaluate non-invasively the hemodynamic response of CRT therapy in heart failure patients.

1051-257 **Patients with Ischemic Cardiomyopathy Have Variable Regions of Latest Activation: Implications for Resynchronization Therapy**

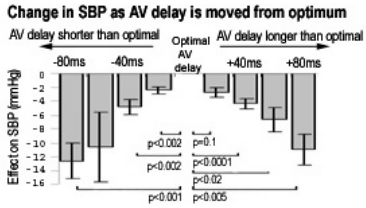
Stuart Beldner, William H. Sauer, Melissa L. McKernan, David Lin, Ralph J. Verdino, Joshua M. Cooper, Henry H. Hsia, David J. Callans, Francis E. Marchlinski, University of Pennsylvania Health System, Philadelphia, PA

Background: Patients with ischemic cardiomyopathy, increased QRS duration, and congestive heart failure benefit from biventricular pacing. The optimal site for placement of the left ventricular (LV) lead is unclear. It has been suggested that the basal lateral wall should be targeted for LV pacing, but the optimal pacing site likely varies, depending on the impact of myocardial scar. We sought to identify the region of latest activation in patients with ischemic cardiomyopathy and prolonged QRS to characterize the variability of electrical dysynchrony.
Methods: Fifteen consecutive patients with ischemic cardiomyopathy and QRS duration > 120 ms, undergoing electrophysiology testing and ablation of ventricular tachycardia were included in the study. All patients had LV activation and voltage mapping in sinus rhythm. Myocardial scar was defined as voltage < 1.5mV and all activation times were recorded using electroanatomical mapping with a 4 mm catheter (Carto, Biosense-Webster; mean number of points 293 +/- 120). One-way analysis of variance and bivariable correlation were used to compare assigned regions of latest activation and clinical characteristics of the cohort.
Results: The mean LV ejection fraction was 22.7 +/- 7.8% and the mean QRS duration for all patients was 142.7 +/- 18.3 ms (10 LBBB: 144.9 +/- 19.2 ms; 5 RBBB: 138.2 +/- 17.3 ms). There were 9 different regions of latest activation with the apex and basal lateral wall most common (4 patients each; 26.7%). There were no electrophysiologic or clinical characteristics that predicted the region of latest activation (P>0.05).
Conclusions: Patients with ischemic cardiomyopathy have variable regions of late left ventricular activation. These results may have implications for cardiac resynchronization therapy.

1051-258 **Continuous Non-Invasive Hemodynamic Monitoring to Optimize Atrioventricular Delay in Cardiac Resychronization Therapy**

Zachary I. Whinnett, Justin E.R Davies, Keith Willson, Anthony W. Chow, Rodney A. Foale, D. Wyn Davies, Alun D. Hughes, Darrel P. Francis, Jamil Mayet, Imperial College, London, United Kingdom, St May's Hospital, London, United Kingdom

Background: The atrioventricular (AV) delay of cardiac resynchronization devices should be optimized after implantation. Use of echocardiography for this purpose is technically demanding and time-consuming. We studied the use of continuous measurement of instantaneous changes in systolic blood pressure (SBP) as an alternative.
Methods: The effect of differing AV delays (40 - 240ms) on beat-to-beat SBP was examined using a validated non-invasive finger photoplethysmograph device (Finapres). 12 patients (median age 70; 8 male) with biventricular pacemakers were studied. Multiple alternations were performed and averaged to allow a precise measurement of SBP for each AV delay setting. The SBP at each AV delay was normalized to values at an AV delay of 120ms and the optimum AV delay was defined as that yielding the maximum normalized increase in BP (SBP). Data are means ±SEM.
Results: The optimal AV delay varied between individual patients (median 160 range 120 - 200 ms). An AV delay 40ms less than the individual's optimum reduced SBP by 4.9±1.1 mmHg (p<0.003); and a delay of 40ms above optimal decreased SBP by 4.4±0.73 mmHg (p<0.0005). Changes in AV delay exceeding 40ms caused SBP to fall even further (Figure).



Conclusions: Small changes in AV delay produce significant hemodynamic effects detectable by noninvasive blood pressure measurements. The ease and acceptability of this non-invasive approach makes it potentially useful as a clinical tool.

1051-259 **AV Delay Programming and Cardiac Resynchronization Therapy: Left Ventricular Diastolic Filling Indices and Relation to Stroke Volume**

Alan D. Waggoner, Mitchell N. Faddis, Judy Osborn, Joann Reagan, Sharon Heuerman, Victor G. Davila-Roman, Washington University, St. Louis, MO

Background: Pulsed Doppler mitral inflow velocities are used to optimize AV delay (AVD) during cardiac resynchronization therapy (CRT). Whether optimizing AVD to improve left ventricular (LV) diastolic filling is related to optimizing the AVD that increases LV stroke volume (ie, aortic time velocity integral, AoTVI), has not been characterized.
Methods: 31 patients (age 57 ± 11 years, 21 male, LV ejection fraction: 25 ± 5%) were evaluated by Doppler measurements of AoTVI, mitral early (E) and late filling (A) velocities, E and A duration (dur), and diastolic filling time (DFT) pre-CRT, and at AVD of 60-160 ms (20 ms increments) after 10 cardiac cycles of pacing (acute-CRT). The AVD that maximally increased AoTVI, mitral E-wave duration, mitral A-wave duration, or DFT was considered "optimal."
Results (see table): The optimal AVD by the AoTVI method was longer compared to optimal AVD that increases E wave duration or DFT (both p = .001) but was similar to

the AVD that increased mitral A-wave duration. Optimal AVD by the AoTVI method was shorter in patients with pre-CRT mitral E/A velocity ratio < 1 (n = 13) compared to those with E/A ≥ 1 (n=18, 97±37 vs.127±24 ms, respectively, p = .01); relative increase of AoTVI was lower in patients with E/A < 1 compared to E/A ≥ 1 (11 ± 12 vs. 22 ± 12%, p = .02).
Conclusions: In CRT patients the AVD that increases LV diastolic filling time differs significantly from that which improves stroke volume. The LV diastolic filling pattern pre CRT influences the optimal AVD in heart failure patients.

	AoTVI (cm)	E dur (ms)	A dur (ms)	DFT (ms)
Pre-CRT	19.7±5.9	181±48	129±37	353±94
Acute-CRT	22.7±5.7	268±65	146±29	441±92
p value (pre- vs acute-CRT)	<.001	<.001	<.001	<.001
Optimal AVD	114±33	83±29*	123±36	84±32*
mean ± SD; * p < .001 vs. optimal AVD by AoTVI				

1051-260 Beneficial Chronic Effects Of AV-Delay Optimization In Patiens With Cardiac Resynchronisation Therapy

Stefan E. Hardt, Said Hashem Fani Yazdi, Alexander Bauer, Arthur Filusch, Philipp Ehlermann, Peter Staritz, Grigorios Korosoglou, Alexander Hansen, Andrew Remppis, Wolfgang Schoels, Hugo A. Katus, Helmut F. Kuecherer, University of Heidelberg, Heidelberg, Germany

Background: Cardiac resynchronisation therapy (**CRT**) has become a valuable treatment option in selected patients with heart failure. Acute changes of the AV-Delay in CRT patients have a significant impact on hemodynamics. However, the more important chronic functional effects of AV-Delay optimization have not been systematically examined despite of its potential role for chronic functional improvement. Furthermore, there is no chronically validated standard procedure for optimizing AV-Delay.
Aims: Therefore, in this study we investigated whether optimization of AV-Delay in CRT patients as assessed by echocardiographic measurement of the velocity time integral of the left ventricular outflow (**LVOT-VTI**) chronically changes 1. walking distance in the 6 min walk test, 2. levels of NT-proBNP as a marker of heart failure and 3. echocardiographic parameters of left ventricular function. 16 patients were enrolled in this study (15 male) aged 63±2 years, who had dilated (n=10) or ischemic cardiomyopathy (n=6). Optimization was performed 43±13 weeks after initiation of CRT. Follow up (**FU**) was conducted 39±2 days after optimization.
Results: LVOT-VTI increased from 188±11 mm (baseline) to 207±13 mm (optimized conditions, p<0.05). Compared to initial values AV-Delay was reduced by 43±8 ms in 9 patients and prolonged by 29±3 ms in 7 patients using this method of optimization. 6 min walk test improved from 442±17 m (baseline) to 479±18 m at FU (p<0.05). During this period NT-proBNP significantly decreased from 3016±990 ng/l to 1862±545 ng/l by 25 %. There was a slight but significant increase of LV-ejection fraction as assessed by echocardiography acutely after optimization (baseline: 27±2%, optimized: 30±2%, p<0.05), while LV-ejection fraction at FU (28±3%) did not differ from baseline. Furthermore, the peak systolic velocity of tissue doppler imaging of the septal and the lateral mitral anulus did not differ significantly between baseline, post-optimization and at FU.
Conclusion: This study demonstrates for the first time chronic functional improvement due to AV-Delay optimization guided by echocardiographic measurement of LVOT-VTI in patients with CRT.

1051-261 Comparison of Single-Site and Regional Pacing: Implications for Resynchronization Therapy

Robert H. Helm, Amir Schricker, Samantapudi Daya, James Chen, Richard Tunin, Menekhem Zviman, Ronald Berger, Henry Halperin, David Kass, Albert Lardo, Johns Hopkins Medical Institution, Baltimore, MD

Background: Ventricular stimulation during both single and dual chamber cardiac resynchronization therapy (CRT) is achieved using single-site electrodes that produce point source stimulation. It remains unknown, however, whether single-site stimulation (SS) or multi-site regional stimulation (RS) produces a greater chamber function response. The purpose of this study was to systematically compare acute chamber hemodynamics during SS and RS pacing using a novel electroanatomic mapping and multi-site stimulation setup.
Methods: An elastic mesh sock, containing 128 evenly distributed stimulation/recording electrodes was fitted over the ventricular epicardium of 8 canines. RS consisted of a patch of 4-6 single electrodes dispersed over approximately 4-10 cm^2. The single electrode centered in the RS field was used for SS pacing. The pacing scheme consisted of baseline right atrial pacing (RAP) followed by a randomly selected ventricular pacing sequence: SS or RS of the right ventricular free wall (RV), apical region (AP), and left ventricular free wall (LV). Systolic function was measured for each pacing scheme using an intracardiac pressure catheter and was expressed as a percent change in dP/dt_{max} from baseline RAP.
Results: Each pacing scheme produced a decrease in dP/dt_{max} (more dyssynchrony) from baseline (average of -15.2% ±1.1). RS of the RV, AP, and LV produced a greater percent decrease in dP/dt_{max} (greater dyssynchrony) than SS pacing of the same region (relative difference of 19.8 ± 1.3%, 60.0 ± 1.6%, 55.4% ± 1.3%, respectively) with all p <0.05.
Conclusion: SS generates superior chamber hemodynamics as compared with multi-site RS pacing in RV, AP, and LV regions. Decreased function during RS may be attributed a reduction in mechanical wave propagation due to simultaneous stimulation of a large region of myocardium that then becomes more susceptible to late-systolic stretching. Further studies using a tagged-MRI motion analysis are needed to further evaluate the mechanical effects of regional stimulation.

1051-262 Greater Sensitivity of Cardiac Function to Ventricular Pacing Lead Location in Patients With vs. Without Left Ventricular Dysfunction

Randy Lieberman, Luigi Padeletti, William Eastman, Douglas A. Hettrick, Harper Hospital, Detroit, MI, University of Florence, Florence, Italy

Background: Results of pacing trials comparing right ventricular (RV) and left ventricular (LV) lead location have been equivocal and may depend on the population studied. We compared LV function during acute RV, LV and bi-ventricular (BiV) pacing in patients with vs. without LV dysfunction. Methods: LV pressure and volume data were recorded during electrophysiology study in 20 patients prospectively stratified by (High) LV ejection fraction (EF) ≥ 35% (n=14; 63±12 y; 4M; EF=28±4%) or (Low) EF < 35% (n=6; 65±11 y, 3M; EF=52±12%). QRS width was 95±13 and 93±18 ms, respectively. Constant atrial overdrive pacing was maintained (78±13 bpm). LV pressure and volume were measured via a pressure-conductance catheter during acute dual chamber pacing from the RV apex, RV free wall, RV septum, LV and BiV(LV- RV septum). AV delay was programmed to the atrial-pace to His potential interval minus 10 ms to avoid fusion. Stroke work (SW), stroke volume (SV), ejection fraction (EF), +dP/dt, efficiency (SW/SV) and synchrony index (SYN) were compared between sites and between groups. Results: Multiple indices of LV function including SW, SV, +dP/dt, EF, LVSP, SW/SV and SYN varied significantly (p<0.05) with pacing site. Also, the mean coefficient of variation for different pacing sites was lower in the High EF group for multiple indices of LV function (Table). Conclusions: RV and LV pacing sites may have greater impact on acute LV function in populations with more severe LV dysfunction. Long term outcome trials are ongoing.

Variability in LV Function Indices

Coefficient of Variability	High EF (n=14)	Low EF (n=6)	p
SW	15.9±9.1%	27.1±6.4%	0.01
SV	16.3±8.4%	22.1±7.3%	0.16
SW/SV	5.5±3.5%	11.4±6.5%	0.02
+dP/dt	6.0±3.7%	11.8±4.4%	0.01
LVSP	4.9±3.1%	13.5±7.3%	<0.01
SYN	15.2±6.5%	20.0±7.7%	0.17

POSTER SESSION

1078 Thrombotic Risk in Atrial Fibrillation

Monday, March 07, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 9:00 a.m.-10:00 a.m.

1078-257 Platelet Activation Promotes Formation Of Platelet-Leukocyte Conjugates (PLC) In Non-Valvular Atrial Fibrillation (AF)

Julio A. Chirinos, Aurelio Castrellon, Juan P. Zambrano, Wenche Jy, Lawrence L. Horstman, Eugene R. Ahn, Joaquin J. Jimenez, Howard Willens, Agustin Castellanos, Robert J. Myerburg, Yeon S. Ahn, University of Miami School of Medicine, Miami, FL

Background: Increased platelet and leukocyte activation have been reported in atrial fibrillation (AF). Formation of platelet-leukocyte conjugates (PLC) is an important mechanism by which leukocytes contribute to thrombosis. The mechanisms driving the formation of PLC in AF are unclear. We investigated the levels of PLC, platelet expression of P selectin, and leukocyte activation in patients with non-valvular AF.
Methods: We studied 14 patients with chronic AF (mean age=62.9 years) and compared them to normal controls. Since we have shown that digitalis use is associated with platelet activation in AF, patients taking digitalis were excluded. We used flow cytometry to measure platelet expression of P selectin and leukocyte expression of CD11b. Coexpression of CD41 and CD45 was used to measure PLC.
Results: Comorbidities included hypertension (85%), diabetes mellitus (21%), coronary artery disease (35%) and congestive heart failure (28%). The mean heart rate was 80 bpm. The mean BP was 127 / 75 mmHg. The mean left ventricular ejection fraction was 49%.All patients were taking warfarin and 78% were taking aspirin. Patients with AF had markedly increased levels of P selectin (22.1 vs 5.0 FU; p=0.008), PLC (61±13% vs 43±21%; p=0.001) and CD11b expression in leukocytes (16.4 vs. 7.9 FU; p=0.0003). PLC strongly correlated with P selectin expression (R= 0.80; R^2=0.64; p<0.001) but not with leukocyte activation as measured by CD11b expression (R=0.41; R^2= 0.17; p=0.14).
Conclusions: Our findings indicate that (1) Patients with AF demonstrate increased levels of platelet and leukocyte activation; (2) Increased PLC formation occurs in AF; (3) Levels of PLC closely correlate with platelet activation but not with leukocyte activation, suggesting than PLC formation is driven by platelet activation rather than by leukocyte activation in this population. Clopidogrel, but not aspirin, has been shown to decrease the formation of PLC. Our data suggests that aspirin use in AF patients would not be anticipated to normalize platelet activation and PLC formation in AF patients, but other therapies aimed at decreasing PLC formation might decrease the thrombotic risk in AF.

1078-258 Role of Follow-Up Transesophageal Echocardiography Before Elective Cardioversion in Patients With Atrial Fibrillation, Left Atrial Thrombus, and Effective Anticoagulation

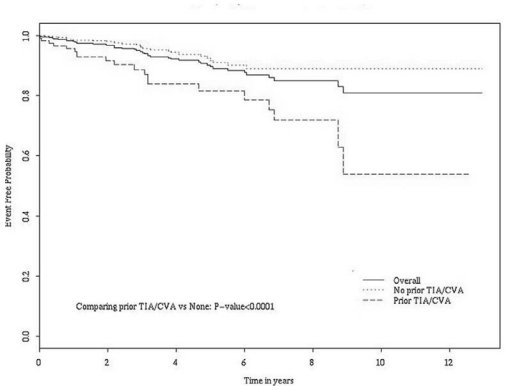
Mohammad Saeed, Atiar Rahman, Giuseppe Augello, Adeel Afzal, Praveen Jammula, Ildiko Agoston, Yochai Birnbaum, Salvatore Rosanio, University of Texas Medical Branch, Galveston, TX, San Raffaele University Hospital, Milan, Italy

Background The value of transesophageal echocardiography (TEE) to prevent cardioversion-related thromboembolic events in patients with atrial fibrillation (AF) and pre-existing atrial thrombus is unclear. We compared the embolic risk associated with a strategy of follow-up TEE-guided direct-current cardioversion (DCCV) with that of blind DCCV in patients with AF, pre-existing thrombus and effective anticoagulation.
Methods We identified 67 subjects with left atrial appendage (LAA) thrombi from a total of 520 consecutive patients with symptomatic non-rheumatic AF who were referred to us for elective DCCV. All patients received at least 4 weeks of adjusted-dose warfarin (target international normalized ratio, 2 to 3) before DCCV. At time of DCCV, 20 patients had follow-up TEE and 47 did not. After DCCV, all patients received warfarin for at least 6 weeks.
Results There were no clinical and echocardiographic differences between the two groups. After a median follow-up of 6 weeks from DCCV, two thromboembolic events were observed in patients who were blindly cardioverted and one in patients in whom the follow-up TEE strategy was used. By multiple logistic regression analysis the TEE strategy was not associated with a lower risk of thromboembolism as compared to blind DCCV (odds ratio 1.37; 95% confidence interval, 0.16% to 15.86%; p = 0.20). Thrombus resolution and no further formation occurred in all TEE patients but two (90%).
Conclusions In patients with AF, LAA thrombi and effective anticoagulation, there is no difference in the risk of clinical thromboembolism between DCCV with or without follow-up TEE. Benefits of warfarin are related to thrombus resolution and prevention of new thrombus formation. Cost analysis data will be soon available.

1078-259 Atrioventricular Nodal Ablation and Permanent Pacing Does Not Increase the Risk of Stroke in Atrial Fibrillation

Lin Y. Chen, Cevher Ozcan, Mahek Mirza, Jane M. Trusty, Peggy L. Weivoda, David O. Hodge, Arshad Jahangir, Win K. Shen, Mayo Clinic, Rochester, MN

Introduction: Although we previously showed that the survival of atrial fibrillation (AF) patients who underwent atrioventricular nodal (AVN) ablation was similar to patients on drug therapy, the stroke risk after AVN ablation is unknown. We hypothesized that AVN ablation per se, does not increase stroke risk in AF.
Methods: We studied all patients with AF who underwent AVN ablation and pacing between 1990 and 2002. The stroke risk was estimated by the Kaplan-Meier method. Multivariate predictors for stroke were identified using a stepwise Cox proportional hazards model.
Results: A total of 605 patients (male 50.7%, mean age 69.5 ± 11.0 years, mean ejection fraction 48.1 ± 16.9%) were followed for a mean duration of 3.8 ± 2.9 years. The cumulative stroke risk at 8 years was 15% (95% CI, 10% to 20%)(Figure). Based on historical controls, the annual stroke risk in AF patients on warfarin is 1.9%. The use of warfarin after AVN ablation was 66.6%. The proportion of patients with hypertension and history of TIA/stroke were 55.2% and 20.2% respectively. The multivariate predictors for stroke were history of TIA/stroke (p=0.0003) and not using warfarin (p=0.0098).
Conclusion: The stroke risk in our study is comparable with the stroke risk in AF patients on warfarin as reported in past trials. AVN ablation per se, does not increase stroke risk in AF. Warfarin should be continued for stroke prophylaxis after AVN ablation.



1078-260 Risk Of Thrombus Formation And Development Of Pulmonary Venous Obstruction After Percutaneous Left Atrial Appendage Occlusion

Heyder Omran, Harald Schmidt, Christoph Hammerstingl, Giso von der Recke, Berndt Lüderitz, David Hardung, St.-Marien-Hospital, Bonn, Germany, University of Bonn, Bonn, Germany

Background: A new interventional occlusion system for the left atrial appendage (PLAATO) has been introduced as an alternative treatment in patients with increased thromboembolic risk due to atrial fibrillation (AF) and contraindications for oral anticoagulation (OAC). Occlusion of the left atrial appendage (LAA) may compress the left pulmonary vein and carries the risk of thrombus formation on the surface of the device. The aim of this prospective study was to evaluate the morphological and hemodynamical changes following the procedure by means of serial transthoracic and transesophageal echocardiographic examinations.
Methods: 34 patients with persistent AF were included in the study. Echocardiographic examinations were performed 24 hours prior to the procedure, during the occlusion procedure, prior to discharge of the hospital, after 1, 2, 6, 12 months and after 2 years. The echocardiographic analysis included the following parameters: size of the LAA prior to and after the procedure, peak pulmonary vein flow and presence of thrombi on the surface of the device.
Results: The average size of the LAA area was 5.92 ± 2.07 cm^2 prior to and 0.78 ± 0.49 cm^2 after implantation of the device ($p < 0.0001$). Presence of thrombi could be documented neither on the surface of the occluding device nor in the left atrium during the complete follow-up period. Peak flow velocities of the pulmonary veins were not significantly higher after the positioning of the occluding device (0.60 ± 0.15 prior versus 0.67 ± 0.14 m/s after the occlusion, p = ns).
Conclusion: The implantation of a new percutaneous left atrial appendage occlusion system reduces the size of the LAA significantly. Thrombotic appositions on the device were not documented in the follow-up period and obstruction of the left pulmonary vein was not observed after implantation of the device.

1078-261 Percutaneous Occlusion Of The Left Atrial Appendage: Cerebral Magnetic Resonance Imaging To Determine Long Term Risk Of Cerebral Embolism After The Procedure

Heyder Omran, Harald Schmidt, Christoph Hammerstingl, Giso von der Recke, Berndt Lüderitz, David Hardung, St.-Marien-Hospital, Bonn, Germany, University of Bonn, Bonn, Germany

Background: Percutaneous left atrial appendage occlusion has been introduced as an alternative treatment in patients with atrial fibrillation and increased thromboembolic risk. However, the long term risk of cerebral embolism under this new treatment is unknown. The aim of the study was to evaluate the long-term risk of cerebral embolism by serial cerebral MRI scanning.
Methods: 34 Patients with contraindications to warfarin or bleeding complication under oral anticoagulation were enrolled in the study. Serial neurological and echocardiographic examinations were undertaken prior to and during the procedure and in addition at 1 month, 2 months, 6, 12 and 24 months. Cerebral MRI including diffusion weighted sequences was performed prior to the procedure, 48 hours after and 6, 12 and 24 months after the procedure to assess for cerebral microembolism.
Results: Cerebral MRI performed prior to the occlusion procedure detected the presence of former cerebral embolism in 12 out of the 34 patients. Follow-up MRI studies excluded the presence of new cerebral microembolism in all patients. TTE and TEE examinations did not reveal de novo thrombus formation in the LA or thrombotic appositions on the surface of the occlusion device during the follow-up period.
Conclusions: Long term follow-up of patients with occlusion of the left atrial appendage did not reveal cerebral thromboembolism. Percutaneous left atrial appendage occlusion is an alternative treatment in patients at high risk of thromboembolism and contraindications to oral anticoagulation therapy.

1078-262 Histopathological Study of Thrombogenesis in Left Atrial Appendage Obtained at the Operation for Atrial Fibrillation

Tsunenori Saito, Koichi Tamura, Mayuko Togashi, Daisuke Uchida, Tomonari Saito, Yuichi Sugisaki, Nippon Medical School, Tokyo, Japan

Background: Thromboembolism is a most important complication to provide the prognosis of patients with atrial fibrillation (AF). To evaluate the mechanism of thrombus formation, histopathological changes including localization of thrombi in resected left atrial appendages (LAA) of valvular AF patients were investigated.
Methods: Clinicopathological studies were made on 56 AF cases: 30 with mitral regurgitation (MR), 3 with mitral stenosis (MS), and 23 with MSR. Pathological findings of thrombi in LAA were compared with clinical features, including history of valvular diseases and embolism, and findings of echocardiography (UCG). Results were analyzed by Chi square test, Fisher's exact method or Welch's t test.
Results: LAA thrombi were categorized into 2 types. Membranous thrombi (M-thrombi) that widely attached and organized to collagenous neointima were found on LAA endocardium in 49 patients (88%). Polypoid-shape thrombi (P-thrombi) were observed on M-thrombi in 15 patients (27%). Fresh P-thrombi were found on the ruptured old thrombi in 4 cases. P-thrombi were seen in patients with large left atrials (58 ± 12 vs 50 ± 11 mm; $p < 0.05$); a larger number of MS and MSR patients had P-thrombi in LAA than MR cases (42 vs 13%; $p < 0.05$). Patients with P-thrombi had higher prevalence of past embolism (50 vs 19%; $p < 0.025$) and longer duration of valvular disorders as the basal disease (18 ± 20 vs 8 ± 10 years; $p < 0.05$). Patients with MS had no peculiar localization of thrombi in LAA cavity, but in MR cases, more patients had thrombi in the orifice than the tip of LAA (35 vs 19%; $p < 0.01$). In UCG, MR flow was classified into 3 directions: hitting roof, anteroseptal, and posterolateral wall of the left atrium. Patients that MR flow jet struck posterolateral wall near the entrance of LAA had a higher rate of LAA thrombi than others (57 vs 20%; p = 0.016).
Conclusion: The development of LAA thrombi is influenced by blood stasis and/or direction of MR flow in the left atrium. Great majority of patients with AF have M-thrombi in LAA that are difficult to find by UCG. Instability of M-thrombi including surface rupture before complete organization relates to P-thrombi formation which results in high incidence of embolism in AF patients.

POSTER SESSION

1079 Permanent Pacemakers: Effects, Programming, and Implantation Techniques

Monday, March 07, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 9:00 a.m.-10:00 a.m.

1079-247 The Mechanical Effect of Biatrial Delivery of Non-excitatory Electrical Current.

Joseph Y.S. Chan, Jeffery W.H. Fung, Hamish C.K. Chan, Winnie W.L. Chan, Henry C.M. Yu, John E. Sanderson, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, Hong Kong

Background: Nonexcitatory (NE) electrical current applying to the ventricle improves myocardial contractility and attenuates ventricle remodeling in animal heart failure models. The aim of the study is to investigate the effect of NE electrical current on human atrium.
Methods: 10 patients were recruited (8 females and 2 males, age 45.8±8.5 years). Echocardiogram of left atrium with measurements of peak atrial systolic velocity (AM) at the annulus level and atrial strain rate (SR) were performed after 5 minutes of steady pacing at 4 protocols as shown in the table below. Biatrial pacing at high right atrium and distal coronary sinus (lateral left atrium) through distal poles of endocardial pacing catheters at rate above the intrinsic heart rate were performed at twice diastolic threshold. NE electrical current was commenced by introduction of a 20mA at 2.0msec pulse width electrical impulse at 50msec (refractory period) after every preceding captured pacing impulse.
Results: Using one-way ANOVA analysis it was shown that NE current significantly increased the atrial strain rate of both septal and lateral left atrium when compare to baseline.

* = p<0.05	Baseline	Biatrial pacing	Biatrial pacing +NE	Isoprenaline
Septal AM (cm/sec)	4.25±1.01	5.16±1.26	5.63±6.96*	7.63±1.25*
Lateral AM (cm/sec)	3.26±1.80	3.96±1.44	5.84±2.27*	5.78±1.74*
Septal SR (sec^{-1})	2.29±0.73	2.89±1.23	4.59±1.50*	3.65±1.28
Lateral SR(sec^{-1})	1.73±1.09	2.38±1.41	3.37±1.46*	3.02±1.18

Conclusions: Biatrial delivery of NE current improved global atrial contraction and the effect was observed even at site (left atrial septum) distant from the application sites of NE current (lateral left atrium).

1079-248 Detection of Asymptomatic Atrial High Rate Events in Patients with Dual Chamber Pacemaker and Its Prognostic Significance

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Background: The advent of dual chamber pacemakers with mode switch algorithms for detection of atrial high rate events (AHRE) have made the surveillance of atrial tachyarrhythmias feasible. Data regarding the clinical significance of these events is still unclear. The purpose of the current study was to correlate AHRE with clinical variables and outcomes.
Methods: 101 consecutive patients from our pacemaker clinic were evaluated for occurrence of AHRE. Patients with a history of atrial fibrillation (AF) and pacemakers set in a VVI mode were excluded from the analysis (N= 9). A total of 92 patients were then followed prospectively for 18± 9.3 months. Statistical analysis was done using chi- square test for discrete and ANOVA for continuous variables.
Results: The mean age of the patient population was 70 ± 13 years of which, 45% were females, 87% hypertensives, 22% diabetics, 22% with coronary artery disease (CAD) and 32% with congestive heart failure (CHF). Patients with AHRE were older patients than those without AHRE (73 ±12 vs. 64 ±14; p = 0.001). There was no significant difference in the number of AHRE in patients with regards to CAD, DM, or HTN. There were increased AHRE in patients with CHF (950 ± 4,710 vs. 5,961 ± 17,819; p = 0.03). Sub-group analysis of the patients with CHF showed a consistent increase in AHRE in patients with non-ischemic cardiomyopathy (9,458±23,264 vs. 1,049 ± 4,714; P = 0.004). Worsening CHF was associated with gradual but significant increase in the number of AHRE (none or mild- 950 ± 4,710 vs. moderate-5,080 ± 17,549 vs. severe-13,006 ± 22,407; p value = 0.05). During the follow-up period, patients with higher number of AHRE had more hospitalizations for cerebrovascular events (CVA), CHF and AF (p = 0.04). Longer duration (>24 hrs) of AHRE however, was not associated with increased hospitalization.
Conclusion: Patients with increased AHRE irrespective of its duration had an increased incidence of hospitalization for CVA, CHF and AF. Interestingly, CHF was not only associated with increased AHRE but a "dose response" curve was also noticed. AHRE as a surrogate for worsening CHF would be an exciting and, as yet, unexplored hypothesis.

1079-249 Withdrawal or Maintenance of Warfarin Therapy Guided by Implantable Device Datalogs in Patients With Refractory Atrial Fibrillation: A Novel Application of Device Monitoring in Recurrent Atrial Fibrillation

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Background: An increased incidence of stroke has been observed in AF pts who do not maintain warfarin (W) therapy even when a rhythm control (RC) strategy has been attempted. This may be due to incomplete RC or increased risk of thromboembolism due to the underlying disease. We examined the hypothesis that an objective device based documentation of RC or lack thereof can help guide W therapy. **Methods:** We used dual site right atrial pacemakers (DAP) in combination with antiarrhythmic drugs (AAD) &/or catheter ablation i.e. "hybrid" therapy in 113 pts with symptomatic paroxysmal (n=70) or persistent/permanent AF (n=43), mean age 69±9 yrs, mean LA diameter of 42±8 mm, mean LV ejection fraction 47±14 %, refractory to 2±1 AAD. W was continued until pacemaker datalogs confirmed restoration of stable RC without symptomatic or asymptomatic sustained AF for 1 yr.
Results: Survival was 92% at 1 yr, 84% at 3 yrs and 80% at 5 years in the study population. 30 pts (27%) were maintained without long-term W therapy based on the above criteria (Gp A) due to withdrawal (n=26), not initiated due to contraindications (n=2) or pt refusal (n=2) while the remainder continued on W (Gp B). These two groups were comparable for age and gender, but the proportion of pts with persistent AF was higher in Gp B (38 pts= 46%) compared to Gp A (5 pts= 17%). Using the device classification of RC control to define W need, the overall stroke incidence was 1.1% per patient year, which is comparable to expected stroke event rates in age matched populations without AF. There were 3 stroke events, none of which occurred in Group A. Stroke events in Group B occured in patients with paroxysmal AF (2 pts) and persistent AF (1 pt) and could be causally related to refusal of W therapy (2 pts) and fatal intracerebral bleeding on W(1 pt).
Conclusions: 1. W therapy guided by device monitoring for recurrent AF was not associated with increased risk of stroke.2. Device monitoring during a RC strategy may confirm continued need for W therapy, possibly due to the detection of asymptomatic AF and has the potential to further reduce stroke rates in AF populations. 3. Long-term W therapy was safely withdrawn in selected pts with prolonged absence of recurrent AF on device monitoring.

1079-250 Do Aspirin and Clopidogrel Increase the Risk of Cardiac Device Implantation?

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Background: Aspirin+Clopidogrel (A+C) represents an increasingly popular combination therapy in patients with coronary artery disease. Its use has recently been associated with excess risk of bleeding following coronary artery bypass surgery. We investigated if A+C results into a higher complication rate following cardiac device implantation.
Methods: This study enrolled 300 patients (pts) undergoing pacemaker (n=169) or ICD (n=131) implantation while on therapy with A alone (118 pts), A+C (71pts), C alone (4 pts) or neither A or C (107 pts). Collected data were analyzed according to the presence or absence of C therapy and then corrected for A exposure.
Results: There was a total of 11 complications, of which 4 occurred in the Group on C therapy (Group I: 3 pocket hematomas, and 1 hemothorax), and 7 in Group off C therapy (Group II: 5 hematomas, 1 pneumothorax, and 1 hemothorax). Groups I and II were comparable in terms of age, gender, body surface area, preoperative platelet count, prothrombin time, activated partial thromboplastin time and creatinine values, as well as procedural times (adjusted according to the device type). Complication rates were similar in both Groups (5.3% vs 3.1%, p= NS). There was a higher prevalence of A exposure in Group I than in Group II (94.6 % vs 52.4 %, p < .0001). Pts with A exposure had longer procedure times (p=0.006) and were more likely to develop complications compared to pts without A exposure. Using a logistic regression analysis model, this difference was statistically significant (5.29 % vs 0.90 %, p= 0.0055, odds ratio of 16.7).
Conclusion: Aspirin exposure is a risk factor for periprocedural adverse events in pts undergoing cardiac device implantation. Combination therapy with Clopidogrel does not significantly increase this risk.

1079-251 The Effects Of Right Ventricular Apex Pacing On Tei Index And Bnp In Patients With A Dual Chamber Pacemaker

Naoya Oketani, Sanemasa Ishida, Shuichi Hamasaki, Kunitsugu Takasaki, Tomoko Ichiki, Manabu Setoguchi, Shin Kawazoe, Yasuhisa Iriki, Makoto Yamashita, Hitoshi Nakashima, Tatsuru Matsuoka, Chuwa Tei, National Hospital Organization Kyusyu Cardiovascular Center, Kagoshima, Japan, Kagoshima University, Kagoshima, Japan

Backgrounds: Synchronous electrical activation, as induced by right ventricular apex (RVA) pacing, causes various abnormalities in left ventricular (LV) function, especially in the context of severe LV dysfunction or structural heart disease. However, the effect of right ventricular apex pacing in patients with normal LV and right ventricular (RV) function has not been fully elucidated. The aim of this study was to characterize the effects of right ventricular apex pacing on LV and RV function by assessing isovolumic contraction time and isovolumic relaxation time divided by ejection time (Tei-index) and BNP.
Methods: Doppler echocardiographic study and the measurement of BNP was performed in 76 patients with dual chamber pacemaker without structural heart disease (30 sick sinus syndrome, 46 atrio-ventricular block). Patients were divided into one of two groups according to the incidence rate of right ventricular apex (RVA) pacing by 24-hour ambulatory ECG that was recorded just before echocardiographic study: group A, n=44, patients with incidence of RVA>=50%, mean pacing rate 99.6 ± 1.5%; group B, n=30, patients with incidence of RVA<50% mean pacing rate 2.5 ± 6.3%.

Results: There was no significant difference in mean heart rate derived from 24-hour ambulatory ECG recordings (66.4 ± 11.3 bpm vs. 68.5 ± 7.5 bpm) when comparing the two groups. LV Tei index in group A was significantly higher than that in group B (0.67 ± 0.17 vs. 0.45 ± 0.09, P<0.0001). And RV Tei index in group A was significantly higher than that in group B (0.34 ± 0.19 vs. 0.25 ± 0.09, P<0.05). And then BNP in group A was significantly higher than that in group B (39.7 ± 46.9 vs. 17.7 ± 11.3, P<0.05). There were no significant differences in other echocardiographic parameters when comparing the two groups, including left atrium diameter (35 ± 8 mm vs. 34 ± 5 mm), LV systolic dimension (30 ± 6 mm vs. 29 ± 7 mm), and ejection fraction (66 ± 9% vs. 63 ± 11%), except of LV diastolic dimension (49 ± 5 mm vs. 45 ± 5 mm, p<0.05). **Conclusions:** These findings suggest that right ventricular apex pacing results in global left ventricular and right ventricular function abnormalities in patients with dual chamber pacemakers.

1079-252 Individual Optimization Of Pacing Sensors Improves Exercise Capacity

Ayten Erol-Yilmaz, Tim A. Schrama, Jutta Schroeder Tanka, Arthur A. Wilde, Jan G. Tijssen, Raymond Tukkie, Academic Medical Center, Amsterdam, The Netherlands

Background: Programmable pacemaker sensor features are frequently used in default setting. Limited data are available about the effect of sensor optimization on exercise capacity and quality of life (QOL). Influence of individual optimization of sensors on QOL and exercise tolerance was investigated in a randomized, single blind study in patients with VVIR, DDDR or AAIR pacemakers.
Methods: Patients with ³ 75% pacing were randomized to optimized sensor settings (OSS) or default sensor setting (DSS). Standardized optimization was performed using three different exercise tests. QOL questionnaires (QOL-q: Hacettepe, Karolinska and RAND-36) were used for evaluation of the sensor optimalization. One month before and after optimalization, exercise capacity using CAEP and the three
QOL-q were assessed.
Results: Fifty-four patients (26 men, 28 female) with a mean age of 65 ± 16 years were enrolled in the study. In each group (OSS and DSS) 27 patients were included. One month after sensor optimization the achieved maximal HR and METS were significantly higher in OSS compared to DSS (124± 28 vs. 108 ± 20 bpm, p=0.036; 7.3± 4 vs. 4.9 ± 4 METS, p=0.045). Highest HR and METS were achieved in patients with pacemakers with accessible sensor algorithms. In patients with automatic slope settings (33 %), exercise capacity did not improve after sensor optimalization. QOL did not improve in OSS compared to DSS.
Conclusion: After 1 month of individual optimization of rate response pacemakers, exercise capacity was improved and maximum heart rate increased, although QOL remained unchanged. Accessible pacemaker sensor algorithms are mandatory for individual optimization.

1079-253 Is Infiltration Of Pacemaker Pocket By Antiseptic Solution Necessary At The Time Of Implant/ Replacement?

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Background: Prophylactic infiltration of pocket with antiseptic solution following device implants is routine during surgical procedure. However its value in preventing infection is not established in cardiac device recipients. We sought to determine in randomized fashion whether such a practice has any benefit in preventing subsequent infections in patients undergoing new pacemaker implant as well as those undergoing generator change.
Methods: Consecutive patients undergoing pacemaker implants at two laboratories at our institution by same operators using same technique of patient preparation and implant procedure were studied. The patients were randomized to either have pocket infiltration with betadine or vancomycin solution ("infiltration group") or no infiltration of pocket ("no infiltration group") during implantation of a new pacemaker system or only generator replacement. All patients received prophylactic intravenous antibiotics followed by oral antibiotics for 5 days under a similar protocol.
Results: Over a period of 30 months 151 patients underwent new pacemaker implant and 27 had a generator replacement in the "no infiltration" group for standard indications. Over a similar period 176 patients had new implant and 39 had generator replacement in the "infiltration" group. Over a mean follow up of 15 months, one patient in "no infiltration" group and two patients in the "infiltration group" had device related infection of the pocket. Of these, 2/3 required explantation of the pacemaker system and subsequent implantation on the contralateral side. All patients who had infection had a new pacemaker system implanted, were diabetics and the infection was apparent within the first three months.
Conclusion: Infiltration of the pocket after pacemaker implantation is unnecessary for either new implants or generator replacements if prophylactic intravenous followed by oral antibiotics are used. Infection rates are low in general and are higher in diabetics.

1079-254 A New Technique For Direct His-bundle Pacing

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Introduction: increased clinical evidences show that conventional right ventricular pacing is detrimental to left ventricular function. A theoretical pacing system that could preserve the normal Purkinje activation should be considered the ideal pacing approach.
Aim of the study: to investigate the safety and the reliability of direct His bundle pacing (DHBP) using a new system composed by a steerable catheter and a new 4.1 Fr. Screw-in lead.
Method: 15 patients (11 male, mean age 76 ± 10 years) with standard PM indication and a narrow QRS were enrolled and DHBP was attempted.
Results: DHBP was achieved in 13/15 patients; in two patients the Hissian area was achieved, but the paced QRS morphology and duration were different form the native ones. The mean time for lead positioning was 27 ± 23 minutes, the mean fluoroscopy time was 20 ± 22 minutes and the total procedure time (skin to skin including the positioning of standard EP catheter for His recording) was 80 ± 33 minutes. In DHBP pacing, acute pacing threshold was 2.6 ± 1.2 V at a pulse width of 0.5 ms., whereas sensed potentials were 3.1 ± 2.2 mV. At one month follow-up the same QRS duration and morphology recorded at implant were observed in all patients, pacing threshold was 2.8 ± 1.8 V, with a ventricular sensing of 3.0 ± 2.0 mV, the sensing configuration was changed from bipolar to unipolar in five patients to solve undersensing issues.
No major complications were observed.
Conclusions: DHBP in patients with narrow QRS and standard PM indications is safe and feasible using a new system composed by a steerable catheter and a new screw-in lead. Further studies are needed to evaluate the clinical impact of this technique.

1079-255 The Effects of VOO Ventricular Pacing on Ventricular Function Using a New Intracardiac Imaging System Developed to Guide Multi-Site Pacing

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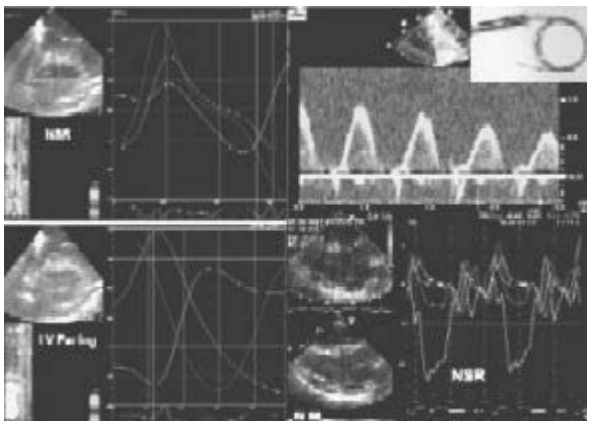
Background: We studied 3 pigs during RV or LV pacing compared to NSR, using as guidance, a new high frequency ultrasound imaging catheter: 9 French with a 64-element, 8-14 MHz, side-looking array. It is highly steerable with diagnostic electrodes and runs on a GE/VingMed Vivid 7 system.
Methods: The device was developed by an NHLBI Bioengineering Research Partnership focused on new tools for intracardiac imaging and interventional therapy. The device was easily introduced from femoral or jugular venous and manipulated without fluoroscopy.
Results: High resolution images with tissue Doppler strain rate were easily obtained from the RA encompassing the whole RV and LV out to 8cm depth. For evaluating synchrony/ asynchrony on LV short axis views, we determined the time between first and last peak systolic SR points on curves from 3 LV sample regions (septum, lateral and inferior walls) for 10 states of LV or RV pacing and compared them to NSR. This time period was 52 ± 17 msec (SD) for LV pacing. The time for peak SR at the same LV regions was shorter during RV pacing (22 ± 7 msec, p = NS) 17 ± 4 msec for NSR (p < 0.01). Lastly, global strain and strain rate determined with a new 2D strain analysis program showed decreased global LV strain during both RV and LV pacing.
Conclusions: This new prototype ultrasound/EP device is easily steerable without fluoroscopy from jugular or femoral venous positions and should be applicable for guiding resynchronization therapy in the cath lab thus possibly reducing fluoroscopy time.



1079-256 Pronounced Left Ventricular Dilation and Scar Tissue Extension Preclude Reverse Remodeling Deriving From Cardiac Resynchronization Therapy In Patients With Ischemic Cardiomyopathy

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Background: Recent studies showed that cardiac resynchronization therapy (CRT) with pacing results in reverse remodeling, improvement in systolic left ventricular (LV) function, functional status and well being of patients with end stage chronic congestive heart failure. However, 20% to 30% of patients may not respond to CRT, particularly if cardiomyopathy is of ischemic origin. We examined the relation between LV features and absence of reverse remodelling after CRT.
Methods: Thirty-tree patients, age 66 ±8, with ischemic cardiomyopathy, NYHA class III or IV despite optimal medical therapy, LV ejection fraction (EF) <35%, LV end diastolic volume (EDV) >85 ml/m2, QRS > 120 ms and left bundle branch block received a biventricular pacemaker. At baseline and 6 months after implantation, we evaluated NYHA class, LV EF, LV EDV and end systolic (ESV) volumes, intra- and inter-ventricular dyssynchrony by equilibribium radionuclide ventriculography phase analysis. Stress and rest (early and 24-h late) myocardial perfusion scintigraphy was performed at baseline.
Results: There were 15 patients with moderately dilated (ESV ≤90 ml/m2) (Group A) and 18 with markedly dilated (ESV >90 ml/m2) (Group B) LV. LV EF (30 ±5 vs 29 ±4; p=0.5, respectively), NYHA class (3.3 ±0.5 vs 3.6 ±0.5; p=0.1, respectively) were similar in Group A and B. EDV (103 ±10 vs 168±9; p<0.0001, respectively), intraventricular dyssynchrony (SD of the LV phase angle: 52 ±14 vs 81 ±14; p<0.0001, respectively) and scar tissue

extension at perfusion scintigraphy (2.4 ±1.1 vs 5.4 ±0.9; p<0.0001, respectively) were smaller in Group A than in group B. There were 14/15 responders to reverse remodelling (reduction in LV ESV ≥15 ml after CRT) in Group A and 6/12 non-responders (<15 ml) in Group B (p=0.05); 14/15 responders to EF (improvement ≥ 5 units after CRT) in Group A and 7/18 non-responders in Group B (p=0.03).
By multiple regression analysis, independent parameters included LVEDV (p<0.01) and the number of scarred segments (p<0.01)
Conclusion: In patients with ischemic cardiomyopathy, a marked LV dilation and extension of scar tissue prevent ongoing LV remodeling after CRT and are associated with lack of LVEF and symptoms improvement

POSTER SESSION

1080 Implantable Defibrillator: Testing and Use

Monday, March 07, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 9:00 a.m.-10:00 a.m.

1080-267 Defibrillator Implantation Testing: How Can Patients Who Require System Modification to Obtain an Adequate Safety Margin for Defibrillation Be Identified?

Andrea M. Russo, William Sauer, Edward Gerstenfeld, David Lin, Henry H. Hsia, Ralph J. Verdino, Hemal Nayak, Joshua M. Cooper, Sanjay Dixit, David J. Callans, Vickas Patel, Francis E. Marchlinski, University of Pennsylvania Health System, Philadelphia, PA

Background*:* Ventricular fibrillation (VF) is typically induced at ICD insertion or replacement. Despite availability of high output devices and biphasic waveforms, some patients (pts) still require system modification (MOD) to obtain an adequate safety margin for defibrillation. If factors predicting MOD were known, testing might be further minimized in some pts.
Methods: We reviewed data on 1085 consecutive pts who underwent ICD implantation with defibrillation threshold (DFT) testing to determine factors predicting MOD. An adequate safety margin was felt to be present if ≥ 2 inductions of VF were effectively terminated with an output ≥10 joules below maximum device output.
Results: An unacceptable safety margin (<10 joule) was identified in 71 pts (6.5%). (Table) Multivariable analysis demonstrated that amiodarone users were >3 times more likely to need MOD (HR:3.35;CI:1.96-5.73, p<0.0001). Non-ischemic disease, younger age, and generator upgrade were also independent predictors of the need for MOD. Long-term mortality was not different between groups (17% versus 20%, p=NS).
Conclusions: In a contemporary population of ICD pts, those at "highest risk" for requiring MOD to obtain an adequate safety margin for defibrillation can be identified. Because "acceptable efficacy" of ICDs in preventing sudden death without testing has not yet been defined, DFT testing remains the standard of care. However, the results provide a starting point to altering these standards in selected pts.

Patients Who Required Modification Vs. Those Who Did Not
(Univariate Analysis):

	Modified (N=71)	No Mod* (N=754)	P value
Age (years)	63 ± 14	66 ± 13	0.021
Female sex (% pts)	26%	25%	0.887
Presence CAD (% pts)	49%	69%	<0.001
Ejection fraction (%)	29 ± 15%	32 ± 14%	0.034
Amiodarone	44%	19%	<0.001
Right-sided implant	10%	5%	0.179
Abdominal generator	6%	6%	1.000
Upgrade/generator replacement	38%	25%	0.024
QRS duration </= 120 msec	42%	50%	0.268

1080-268 Inductionless Defibrillator Implantations

John D. Day, Eric Putz, Demos Iskos, Christopher R. Cole, Curtis Li, David Lyon, Tamara Fritzel, Liz Mino, LDS Hospital, Salt Lake City, UT

Background: Defibrillation threshold (DFT) testing has traditionally been used to ensure that an implantable cardioverter-defibrillator (ICD) can detect and terminate ventricular fibrillation (VF). Testing for the upper limit of vulnerability (ULV) is an alternative method to estimate the DFT that may avoid VF induction. ULV is the weakest shock strength at or above which VF is not induced when a stimulus is delivered during the vulnerable phase of the cardiac cycle. The purpose of the Multicenter Inductionless Defibrillator Implantation Study (MIDIS) was to validate the ULV hypothesis in ICD implantations and allow for potentially inductionless implants.
Methods: 194 patients receiving a Guidant transvenous right ventricular apical dual-coil shocking lead ICD system were recruited from multiple centers. At implantation, ULV screening at 14 Joules (T-wave shocks 20 msec before, 20 msec after, and at the peak of the latest peaking monophasic T-wave) was performed. Patients were considered inductionless if ULV screening at 14 J did not induce VF. Patients with no inducible VF during ULV testing had their initial ventricular tachycardia (VT) and VF therapy programmed at 21 J with the VT/VF detection rate set at 200 bpm (maximum output of ICD was 31 J).
Results: Of the 194 patients included, 151 with a left-sided ICD system were "inductionless" at implantation with ULV screening at 14 J. 100% of these "inductionless" patients who also underwent DFT testing had a DFT ≤ 21 J (n=149, p<0.0001). In those patients who received clinical shocks, and in whom data were available, 10 of these 149 patients (7%) had a total of 19 pre-defined qualifying lower energy shocks for fast VT/VF ≥ 200 bpm during a mean follow-up time of 9.5 months. In 17 of the 19 (89%) clinical shocks, the fast VT/VF was terminated with the first lower energy shock. In the 2 cases where fast VT/VF was not terminated with the first shock, the second shock was successful.
Conclusions: ULV testing is a potentially safer method of ICD testing at implantation that allows for inductionless implantations in most patients. Programming a lower energy first shock for clinical fast VT/VF episodes based on inductionless ULV testing at implantation appears to be safe.

1080-269 A New Step-Wise Approach to Implantable Cardioverter Defibrillator Electrograms Tachycardia Discrimination

Felipe Atienza, Jesús Almendral, Javier García, Mercedes Ortiz, Estrella Munilla, Ana Sánchez, Esteban González-Torrecilla, Angel Arenal, Hospital General Universitario Gregorio Maranon, Madrid, Spain

Background: In patients with Implantable Cardioverter Defibrillators (ICDs), comparison of stored electrograms (EGs) during tachycardia and sinus rhythm (SR) immediately before or after the episode is sometimes not possible/reliable because of limitations of memory capabilities or distortion of EGs after a discharge. We aimed to assess EGs characteristics that could help to distinguish SR/supraventricular tachycardia (SVT) from ventricular tachycardia (VT).
Methods: We evaluated EGs from a variety of models of chronically implanted ICDs from 2 manufacturers (Medtronic & Guidant). The first analysis searched for morphological coincidences in SR EGs of 59 consecutive patients. Then, SR EGs were compared with EGs of 39 VT and 17 SVT. We analyzed the characteristics of the unipolar and bipolar ICD EGs, and their duration and relative timing relationship, both in SR and during spontaneous tachycardia.
Results: SR EG had a consistent morphologic pattern of dominant R wave in 98% of patients, provided a particular ICD model was excluded (in this model 70% had dominant S wave, suggesting a different electronic configuration). Thus all EGs from this ICD model were excluded from further analysis. A dominant S pattern in the unipolar EG was present in 41% of VT-EG, but only 2% of SR-EG, and 7% of SVT-EG (p<0,001). SR-EG morphology was not influenced by bundle branch block (in 25 patients) or infarct location, as demonstrated in a simultaneous 12-lead ECG. The unipolar EG preceded the bipolar EG by a median of 16±15 ms during SR and by 56±26 ms during VT (p<0.001), but no significant difference was found between SR-EG and SVT-EG timing. Duration of unipolar EG or bipolar EG, or bipolar EG morphology did not differ among groups. A multivariate analysis showed that morphology of unipolar EG and EGs timing were significant independent predictors of rhythm mechanism. When the following step-wise approach was used: 1) S wave pattern= VT 2) EGs timing >20 ms=VT, 97% tachycardias were correctly classified.
Conclusions: The proposed step-wise approach could be useful for tachycardia classification of ICD episodes.

1080-270 Reciprocal Relationship between Electrical Storm and Severity of Congestive Heart Failure in Implantable Cardioverter Defibrillator Patients with Dilated Cardiomyopathy

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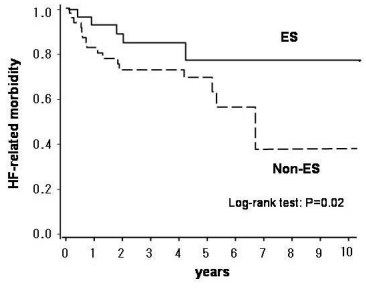
Background: It is suggested that an impaired left ventricular ejection fraction (LVEF) is associated with frequent fires of implantable cardioverter defibrillator (ICD) in pts with congestive heart failure (CHF). However, the relationship between electrical storm (ES) due to ventricular tachycardia/fibrillation (VT/VF) and severity of CHF in ICD pts is not clear.
Methods:We studied 162 pts with dilated cardiomyopathy (DCM; ischemic in 54 and non-ischemic in 108) who were followed for 40±25 months. All pts had LVEF<40% and received ICD for secondary prevention. Clinical characteristics at baseline, HF-related morbidity and total mortality were compared between pts with ES (n=40) and without ES (n=122). ES was defined as ≥ 3 separate episodes of VT/VF within 24 hrs.
Results: There were no statistical differences between pts with and without ES in NYHA class, LVEF, probability of ischemic DCM, and medication use at baseline. However, plasma BNP at baseline in pts with ES was significantly lower than those without ES (164 vs. 328pg/ml, p<0.01). Multivariate analysis elucidated that lower plasma BNP level at baseline was an independent predictor for occurrence of ES (p<0.01). Moreover, HF-related morbidity was significantly lower in pts with ES (p=0.02, Figure), while no significant difference regarding total mortality during follow-up.
Conclusions: This study suggests that presence of ES has a reciprocal relationship with baseline BNP level, and with HF-related morbidity in ICD pts with DCM and VT/VF.

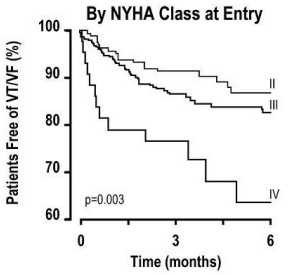


1080-271 **Predictors of Appropriate Defibrillator Therapy in Patients with an Implantable Defibrillator that Delivers Cardiac Resynchronization Therapy**

Aseem D. Desai, Martin C. Burke, Thomas E. Hong, Susan Kim, Yasser Salem, Patrick G. Yong, Bradley P. Knight, University of Chicago Hospitals, Chicago, IL, Guidant Corporation, St. Paul, MN

Background. Little data exists about implantable cardioverter defibrillator (ICD) therapies in patients with NYHA class IV congestive heart failure (CHF), because they have not been considered appropriate candidates for ICD therapy. Our purpose was to determine predictors of ICD therapy in a cardiac resynchronization therapy-defibrillator (CRT-D) population, which includes class IV CHF patients.
Methods. Patients enrolled in the CONTAK CD study were treated with a CRT-D device and required to have class II-IV CHF, QRS duration ≥ 120 ms, and a Class I ICD indication. The database was retrospectively analyzed during the six-month post-implant period to identify predictors of appropriate ICD therapy.
Results. Patients were mostly male (83%), 66±11 yrs old, had coronary disease (69%), mean EF = 0.22±0.07, and class II (33%), III (58%), or IV (9%) CHF. During follow-up, 73/501 (14%) patients received an appropriate therapy. Two independent predictors were identified: a history of spontaneous, sustained ventricular arrhythmias (HR=2.05; 95% CI=1.31-3.20; p=0.002) and class IV CHF (HR=1.81; 95% CI=1.10-2.96; p=0.019).
Conclusions. CRT-D patients with sustained ventricular arrhythmias or class IV CHF are twice as likely to receive an appropriate ICD therapy compared to patients without these factors. This study provides further evidence that advanced CHF is associated with ventricular arrhythmias independent of EF. Further studies are needed to determine if CHF therapy reduces ICD shocks.

Figure. Kaplan-Meier Curves by NYHA Functional Class



Abbreviations. NYHA = New York Heart Association; VT = ventricular tachycardia; VF = ventricular fibrillation

1080-272 **The Influence of Drive Cycle Length on the Initiation of Ventricular Fibrillation During Implantable Cardioverter Defibrillator Threshold Testing: A Prospective Crossover Study**

Neil K. Sanghvi, Paul Lelorier, Arjun Gururaj, Kevin Monahan, Boston Medical Center, Boston, MA

Background: Programmed electrical stimulation of the heart, as a method to induce tachyarrhythmias has been available since the 1960's. To date, no study has examined optimal drive cycle length in the induction of ventricular fibrillation during defibrillation threshold testing after implantable cardioverter defibrillator (ICD) placement. We hypothesized that longer drive cycle lengths, by means of the longer action potential duration, would promote intramyocardial phase 2 reentry and facilitate induction of ventricular fibrillation.
Methods: Fifty consecutive implants were randomized into a prospective crossover format for this study. The group consisted of 40 men and 10 women, each patient receiving either a 400ms or 600ms initial drive train prior to 1.2J internal shock on the T wave with a goal to induce ventricular fibrillation. The timing of the T wave shock was determined by measuring the interval from the beginning of the QRS to the apex of the T wave in lead II. Successful inductions were defibrillated via the ICD. Patients were then crossed over and the protocol repeated. All statistics were calculated using Analyse-It™ for Excel v1.71.
Results: No significant difference existed in age, ratio of males to females, ejection fraction, medications, or patients with diabetes between the drive train groups. Twenty of 23 (87%) patients were successfully induced into VF in the initial 400ms drive train arm whereas 22 of 27 (81%) were successfully induced in the 600ms arm. Thus, a total of 44 out of 50 (88%) patients were successfully induced at 400ms, 41 of 50 (82%) patients were successfully induced at 600ms, and 2 (4%) patients were not inducible at either cycle length. The 2-sided Fisher's exact test returned an insignificant p=0.29.
Conclusion: No investigation to date has questioned whether a relationship exists between drive cycle length and initiation of ventricular fibrillation. Our study addresses this question, though negative for difference between 400ms and 600ms drive trains. Further research into optimal strategies for inducing ventricular fibrillation must be conducted in order to minimize patient sedation time and discomfort while undergoing defibrillator threshold testing.

ORAL CONTRIBUTIONS

806FO Featured Oral Session...Mapping and Ablation of Ventricular Tachycardia

Monday, March 07, 2005, 9:15 a.m.-10:30 a.m.
Orange County Convention Center, Room 230D

9:30 a.m.

806-4 **Tachycardia-induced Cardiomyopathy In Patients With Repetitive Monomorphic Ventricular Ectopy Originating From The Right Ventricular Outflow Tract**

Ravi K. Yarlagadda, Sei Iwai, Kenneth M. Stein, Steven M. Markowitz, Bindi K. Shah, Bruce B. Lerman, Suneet Mittal, Cornell University Medical Center, New York, NY

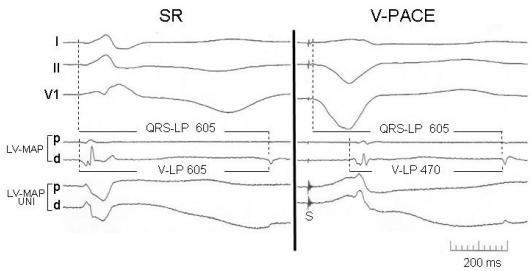
Background: Repetitive monomorphic ventricular ectopy (RMVE) often originates within the right ventricular outflow tract (RVOT). Although usually associated with a good prognosis, isolated cases of tachycardia-induced cardiomyopathy have been reported. We evaluated patients (pts) referred for catheter ablation of RMVE to (1) determine the incidence of tachycardia-induced cardiomyopathy and (2) assess the impact of ablation on left ventricular (LV) function.
Methods: We identified 29 consecutive pts who underwent ablation (using 3D mapping) of RMVE. In all pts, the ectopy had a left-bundle branch, inferior axis morphology. Patients with impaired LV function (EF ≤ 45%) were advised to undergo repeat assessment of LV function following ablation.
Results: The mean age of study pts was 47 ± 15 years (16F, EF 53 ± 11%). Ambulatory 24-hour ECG recordings were available in 21 pts; a mean of 17,843 ± 12,019 premature beats were recorded. Non-sustained VT (up to 18 beats) was seen in 9 pts; no pt had sustained VT. Impaired LV function (40 ± 6 [range: 30-45%]) was present in 10 pts, and was considered idiopathic in 8 pts; the other 2 pts had a prior inferior wall MI. Patients with impaired LV function were more likely to be male (7/13 men, 54% vs. 3/16 women, 19%, p=0.06) and older (58 ± 13 vs. 42 ± 16, p=0.005) than pts with preserved LV function, but there was no difference in the amount of baseline ectopy among groups. Ectopy was successfully ablated from within the RVOT in 25 (86%) pts, including 9 (90%) pts with impaired LV function. Of these 9 pts, 7 had a follow-up assessment of LV function. The EF normalized in all 5 patients with an idiopathic cardiomyopathy; in both pts with an ischemic cardiomyopathy the EF also improved, although the degree of improvement was more limited (3 and 6% increase in EF).
Conclusions: (1) In our referred group of patients with RVOT RMVE, ~1/3 of pts have a tachycardia-induced cardiomyopathy. (2) Ablation should be considered in pts with RMVE, especially those in whom the cardiomyopathy is unexplained, since it may normalize LV function. (3) Younger patients with RMVE should be carefully followed since tachycardia-induced cardiomyopathy may develop over time.

9:45 a.m.

806-5 **Catheter Ablation of Unstable Ventricular Tachycardia Guided by Late Potentials**

Mario D. Gonzalez, Jaime Rivera, Diego N. Velasco, Omer L. Shedd, Keith A. Kyker, Univeristy of Florida, Gainesville, FL

Introduction: Identification of regions of slow conduction during sinus rhythm may facilitate catheter ablation of hemodynamically unstable ventricular tachycardia. We speculated that these regions would show late potentials (LP) with activation times independent of the direction of activation.
Methods and Results: Ablation of multiple, repetitive, hemodynamically unstable, ventricular tachycardias was performed in 12 patients with frequent ICD shocks, late post-myocardial infarction (60±11 year old, 12 males, ejection fraction = 32±7%). Mapping of the left ventricle was performed using the Carto XP system (Biosense Webster). Voltage and activation maps were obtained. Detailed mapping was concentrated in regions showing a voltage ≤ 0.5 mV. Mapping during sinus rhythm was compared with that obtained during right and/or left ventricular stimulation. Late potentials targeted for ablation were those with constant QRS-LP interval independent of the V-LP interval (figure). A total of 22±17 radiofrequency lesions were delivered to eliminate these potentials. All 12 patients were non-inducible at the end of the procedure. After a mean follow-up of 11±4 months 10/12 patients had no recurrence of ventricular tachycardia.
Conclusion: The response to different direction of activation allows identification of late potentials that may participate in reentrant ventricular tachycardias. Ablation of these potentials using radiofrequency current can eliminate un-mapable ventricular tachycardias.



10:00 a.m.

806-6 **Electroanatomic Mapping Characteristics of Ventricular Tachycardia in Patients With Arrhythmogenic Right Ventricular Dysplasia**

Hielko Miljoen, Simona State, Christian de Chillou, Isabelle Magnin-Poull, Pierre Dotto, Marius Andronache, Ahmed Abdelaal, Etienne Aliot, University of Nancy, Nancy, France, University of Antwerp, Antwerp, Belgium

Background: Ventricular tachycardia in arrhythmogenic right ventricular cardiomyopahy/dysplasia has been previously explored using entrainment mapping techniques but little is know about ventricular tachycardia mechanisms and the characteristics of their circuits using an electroanatomical mapping system.
Methods and Results: Three dimensional electroanatomical mapping was performed in 11 patients with well tolerated sustained ventricular tachycardia and arrhythmogenic right ventricular cardiomyopathy/dysplasia. Sinus rhythm mapping of the right ventricle was performed in 8 patients showing areas of low bipolar electrograms voltage (<1.2 mV). In total 12 tachycardias (mean cycle length 382±62 ms) were induced and mapped. Complete maps demonstrated a reentry mechanism in 8 VTs and a focal activation pattern in 4 VTs. The reentrant circuits were localized around the tricuspid annulus (5 VTs), around the right ventricular outflow tract (1 VT) and on the RV free lateral wall (2 VTs). The critical isthmus of the peritricuspid circuits were bounded by the tricuspid annulus and the area of low voltage close to the tricuspid annulus observed during the SR mapping. The isthmus of the RVOT tachycardia was delineated by the tricuspid annulus and a low voltage area localized on the posterior wall of the RVOT. The lateral circuits showed isthmus delineated by two parallel lines of double potentials. Focal tachycardias originated in the RV free lateral wall. Linear radiofrequency ablation performed across the critical isthmus was successful in 7 from the 8 reentrant tachycardias. The focal VTs was successfully ablated in 50% of cases. During a follow up of 9 to 50 months VT recurred in 4 out of 8 initially successfully ablated VTs.
Conclusions: Detailed 3D electroanatomical mapping is helpful in defining the VT mechanism and in reconstructing their circuits in patients with arrhythmogenic right ventricular cardiomyopathy/displasia.

10:15 a.m.

806-7 **Characterization of Arrhythmogenic Substrate and Ventricular Tachycardia Circuits With Non-contact Unipolar Mapping in a Porcine Model of Myocardial Infarction**

Jason T. Jacobson, Valtino X. Afonso, Greg Eisenman, John R. Schultz, John J. Michele, Mark E. Josephson, David J. Callans, University of Pennsylvania, Philadelphia, PA, Harvard University, Boston, MA

Background: Conventional mapping to guide radiofrequency (RF) ablation of scar-based ventricular tachycardia (VT) is limited in patients with hemodynamically untolerated or non-inducible VT. The present study investigates whether non-contact unipolar mapping can define arrhythmogenic substrate and VT circuits.
Methods: 5 pigs underwent experimental myocardial infarction by injection of agarose beads into the distal LAD. After 6 weeks, Dynamic Substrate Mapping (DSM) was performed. This technique defined substrate as the intersection of low voltage areas (< 50% of the largest unipolar deflection recorded in the chamber) identified in sinus rhythm and during pacing from all sides of the infarct. After DSM creation, pacing was performed at 3-5 sites within the substrate to determine the exit sites. RF lesions were placed at sites around the substrate to correlate DSM to gross scar. Programmed stimulation was performed to induce VT. VT was mapped and the circuit defined using standard non-contact mapping techniques. Animals were sacrificed to allow gross examination of the heart. Dimensions of the scar were measured, as were the distances from RF lesions to the scar. DSM was performed in 2 control animals.
Results: Anteroapical substrate and transmural scar were identified in all animals. A mean of 3.2 (2-5) pacing sites were used to construct the DSM substrate. The mean area (±SD) was 16.3 (±7.4) cm^2 by DSM and 14.9 (±8.2) cm^2 by pathology ($p>0.7$). The mean error of measurement of lesion distance from substrate by DSM was 5.4 (±4.4) mm. A mean of 3.6 (2-5) sites were paced within substrate. 10 of 18 sites exited from the substrate adjacent to the pacing area, 7 exited at distant areas and 1 had 2 exits (either side). VT was induced in all animals (mean 1.8 VT morphologies/animal). Except for one VT mapped to the epicardium, all circuit exit sites were located at DSM boundary points. Furthermore, VT circuit exit sites were at (6) or near (3) a pacing exit site. No substrate was identified in the control animals.
Conclusions: DSM is a reliable method of arrhythmogenic substrate localization in this model. Pacing within the substrate can predict VT exit sites and may prove useful for ablation of unmappable VT post MI.

ORAL CONTRIBUTIONS

813 Subcutaneous and Implantable Defibrillators

Monday, March 07, 2005, 11:00 a.m.-12:15 p.m.
Orange County Convention Center, Room 231A

11:00 a.m.

813-3 **Sub-Cutaneous Electrical Defibrillation in Canines**

Riccardo Cappato, Gust Bardy, University of Milan, San Donato Milanese, Milan, Italy, University of Washington, Seattle, WA

Background: We tested the efficacy of electrical defibrillation using a subcutaneous (S)-only electrode approach.
Methods: In 9 dogs (weight 28 ± 3 kg), an initial 8 cm long horizontal incision was created in the 4^{th} to 6^{th} intercostal space along the anterior axillary line. Two pockets were created for placement of a first S electrode (EL) with its leading edge in close proximity to the left edge of the sternum (ST) and a second S electrode at the site of incision along the lateral axillary line (L), such that the two ELs would lay 15±2 cm apart along the same horizontal line. ELs with active surface areas of 5, 10 and 20 cm^2 or with 8 cm-long rod were subsequently positioned in the two pockets and tested for DFT according to different combinations (Table). A custom high output biphasic waveform generator (Cameron Health, Inc.) was connected to the S ELs to conduct S DFT testing following 10 sec-long intervals of VF induced with AC through an endocardial RVA catheter.
Results: Using a step-down skip method for the different configurations, 64 DFT tests with 7 EL configurations were performed. All EL configurations successfully terminated VF. The DFT (delivered energy) in the different EL configurations is summarized in the table.
Conclusion: All investigated S defibrillation configurations proved effective within a range of energies between 10 and 75 J delivered from two ELs lying 15 cm apart in the left hemithorax space. These observations open the way for the development of an S-only implantable defibrillator for human use.

ST/L E (cm^2)	20/5	20/10	20/20	10/5	5/5	5/20	rod 8/20
Mean DFT (J)	65.3	38.2	13.8	30.6	48.9	58.7	39.9
± SD	8.9	16.1	3.7	8.8	26.6	21.4	8.6

11:15 a.m.

813-4 **Feasibility of Left Chest Subcutaneous Electrodes in Terminating Ventricular Fibrillation**

Martin C. Burke, James A. Coman, Adam W. Cates, Curtis C. Lindstrom, David Sandler, Aseem Desai, Bradley P. Knight, University of Chicago, Chicago, IL, Guidant, Inc., St. Paul, MN

Background: The feasibility of a specific subcutaneous (SQ) to cutaneous (Q) anterior left chest vector in terminating ventricular fibrillation (VF) was studied during standard ICD implantation.
Methods: 18 patients (14 male, 63 ± 12 years, LVEF = 28 ± 14) were enrolled and tested with a study vector after intracardiac step down defibrillation threshold testing (DFT) was completed. The study shocks were delivered from a biphasic HeartStart™ (Philips) external defibrillator using an electrode configuration consisting of a SQ active can emulator (Guidant) and a pediatric Q patch electrode (Philips) with an average spacing of 13.3 cm. The SQ active can emulator was placed in the subclavian pocket created for the ICD. The Q patch was placed parallel to the inferior aspect of the heart near the apex as identified with fluoroscopy. An ECD™ (Guidant) was attached to the ICD lead to provide a transvenous defibrillator for rescue shocks. 2 episodes of VF were induced through the ICD lead by rapid pacing or DC current. The defibrillation protocol consisted of 2 stages of patients. In Stage I, the 1st VF episode was treated with 70 joules (J) with a step down (50 J) or step up (100 J) based on outcome. If 50 J shocks were successful in 7/10 patients in Stage I, then testing moved to Stage II. In Stage II, testing began at 50 J with a step down (30 J) or step up (70 J) based on outcome.
Results: Stage I was completed with 7/9 (78%) successes at 70 J (impedance (Z) = 86 ± 20 Ω) and 7/7 successes at 50 J (Z = 85 ± 19 Ω). Of the 2 patients with failures at 70 J, one was immediately converted with 100 J while the other terminated 2 s after the 100 J shock. The ICD DFTs for these 2 patients were 26 J and 6 J, respectively. Stage II was completed with 9/9 successes at 50 J (Z = 78 ± 20 Ω) and 7/9 (78%) successes at 30 J (Z = 80 ± 20 Ω). The ICD DFT for all patients was 10 ± 6.8 J and did not appear to correlate with the study vector defibrillation outcome.
Conclusions: While the majority of patients were successfully defibrillated with < 70J, greater than 10% required 100 J. These data suggest a bimodal distribution of DFT among patients. Further investigation is warranted to understand the population DFT distribution, safety margin requirements, and the need for implant testing.

11:30 a.m.

813-5 **Markers of Arrhythmia Vulnerability Do Not Predict Defibrillator Shocks in Patients With Hypertrophic Obstructive Cardiomyopathy**

Scott W. Burke, Fred A. Crawford, III, William H. Spencer, III, Christopher D. Nielsen, Ron D B Simon, J. Lacy Sturdivant, J. Marcus Wharton, Robert B. Leman, Michael R. Gold, Medical University of South Carolina, Charleston, SC

Background: Hypertrophic obstructive cardiomyopathy (HOCM) is associated with a higher risk of sudden cardiac death (SCD). Arrhythmia markers, including T-wave alternans (TWA), nonsustained VT (NSVT), and inducible ventricular arrhythmias at electrophysiology testing (EPS) predict SCD and defibrillator shocks in some patient populations, but the role of these markers in HOCM is controversial.
Methods: We analyzed 90 consecutive patients with HOCM who underwent alcohol septal ablation and had defibrillators implanted for primary prevention of SCD based on traditional risk factors. These risk factors include family history of SCD, syncope, septal thickness $\geq$ 3.0 cm, and abnormal blood pressure response during exercise. The endpoint was appropriate defibrillator shock.
Results: 64% of patients were male, with a mean age of 48 $\pm$15 years. Mean septal thickness was 2.3 $\pm$0.5 cm and patients had 1.7$\pm$1.1 SCD risk factors. 9 patients had appropriate ICD shocks over a mean follow-up of 23.1 months. Patients receiving shocks were older than those not receiving shocks (59 $\pm$ 16 years vs. 47$\pm$14 years, p=0.01), but septal thickness did not differ between groups (2.1 $\pm$0.5 vs. 2.3$\pm$0.5 cm). There were no significant differences in markers of arrhythmia vulnerability (See Table).
Conclusions: The annual risk of appropriate defibrillator shock was 5.2%. Traditional arrhythmia vulnerability markers did not predict shocks, suggesting that these markers are not useful for risk-stratifying patients with HOCM for SCD.

	TWA +	NSVT	EPS +
Shock	50%	50%	71%
No Shock	50%	62%	83%

11:45 a.m.

813-6 **Different Clinical Characteristics and Worse Outcome in Octogenarians Who Received Implantable Cardioverter-Defibrillators During 2002 - 2003 Compared With 1993-2001**

Lin Y. Chen, Paul A. Friedman, Mudassir Ashraf, David O. Hodge, Arshad Jahangir, Win K. Shen, Mayo Clinic, Rochester, MN

Background Although outcome data are limited in the elderly, ICD utilization continues to grow in octogenarians. In this study, we aimed to determine the clinical characteristics and the survival of octogenarians following ICD implantation before and after MADIT II publication. We hypothesized that a change in clinical characteristics will impact on survival in the very elderly.
Methods All octogenarians who had an ICD implanted at our hospital from 1993 - 2003 were included in the study. The patients were separated into 2 groups as shown in the Table. We chose the cutoff of 2002 as this coincided with MADIT II publication and the expansion of ICD indication for primary sudden death prevention. Categorical and continuous variables were compared using the ^{2} test and rank-sum test respectively. Observed survivals were compared with expected age and sex matched Minnesota population rates. Differences between observed and expected survival were tested using a 1-sample log-rank test.
Results The observed survival in Group 1 was not different from expected (p=0.06), but the observed survival in Group 2 was worse than expected (p<0.001). Compared with Group 1, Group 2 patients were older, had lower EF, and fewer patients for secondary prevention.
Conclusions Octogenarians who had ICD implanted during 2002-2003 had worse survival outcome than those during 1993 - 2001. This was likely due to more implants in patients who were older and with lower EF. More studies to define ICD use in this growing elderly group are needed.

Patients' characteristics, observed and expected survival			
Characteristic	**Group 1 (implanted during 1993 - 2001) (n=70)**	**Group 2 (implanted during 2002 - 2003) (n=76)**	**P value**
Mean age +/- standard deviation(years)	82.7 +/- 2.5	83.1 +/- 2.1	0.04
Male gender (%)	87	79	0.19
Mean Ejection Fraction +/- standard deviation (%)	32.0 +/- 12.7	27.8 +/- 12.1	0.04
Coronary artery disease (%)	70	59	0.17
Ventricular tachycardia (%)	64	43	0.01
Out of hospital cardiac arrest (%)	19	8	0.05
Proportion alive at 2 years [(%) and (95% confidence interval)]	74 (63 to 86)	52 (34 to 79)	0.07
Expected survival at 2 years based on age and sex matched cohort (%)	82	86	

Noon

813-7 **Short QT Syndrome: The Treatment with Implantable Cardioverter Defibrillators is Associated with an Inherent Risk of Inappropriate Discharges**

Rainer Schimpf, Christian Wolpert, Francesca Bianchi, Carla Giustetto, Urs Bauersfeld, Fiorenzo Gaita, Martin Borggrefe, University Hospital Mannheim, Mannheim, Germany, Ospedale Civile Asti, Asti, Italy

Introduction: A congenital short QT-interval constitutes a new primary familial electrical abnormality, which is associated with syncope and/or sudden cardiac death. We report on the performance of implantable cardioverter defibrillator (ICD) therapy in patients with inherited short QT-interval with respect to sensing abnormalities and detection issues.
Methods and Results: In five consecutive patients of two unrelated European families with structurally normal hearts, strong positive family history of sudden cardiac death and excessively shortened QT-intervals ICD devices were implanted for primary and secondary prevention (Atlas VR V-199, n=1, Photon Micro VR-194, n=3, St. Jude Medial Inc, Marquis VR 7230, n=1, Medtroinc Inc.). Mean QT-intervals were 252 ± 13 ms (QTc 287 ± 13 ms). Four of five patients experienced 54 ± 52 days after implantation inappropriate shock therapies for T-wave oversensing despite normal sensing behaviour during intra- and postoperative device testing. In two cases decrease of the R-wave amplitude or an increase of the T-wave amplitude were responsible for the detection of the short coupled T-wave by the automatic sensing algorithm. In one patient revision of the ventricular electrode had to be performed after inadequate shock therapies due to T-wave oversensing after a decrease of the maximal R-wave amplitude < 3 mV. Programming of lower sensitivities and decay delays in 3 of 4 patients prevented further inappropriate discharges.
Conclusions: ICD therapy is actually the therapy of choice in patients with a familial Short QT Syndrome. However, a risk of inappropriate ICD-therapy is inherent due to detection of short coupled and prominent T-waves. Careful testing of ICD-function and adaptation of sensing levels and decay delays without sacrifycing correct arrhythmia detection is essential.

POSTER SESSION

1106 Ventricular Tachycardia: Risk Stratification and Anatomic Substrate

Monday, March 07, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 1:30 p.m.-2:30 p.m.

1106-253 **Long Term Prognostic Value of Electrophysiologic Study After Myocardial Infarction: a Ten Year Follow-Up Study**

Simona Sarzi Braga, Raffaella Vaninetti, Roberto Franco Enrico Pedretti, IRCCS Fondazione Maugeri, Tradate, Italy, TRADATE, Italy

The long-term prognostic power of inducible sustained ventricular tachycardia (VT) at an electrophysiologic study (EPS) performed 1 month after a myocardial infarction (MI) is still unknown. In order to evaluate the long-term prognostic value of inducible sustained VT after MI, we investigated the clinical outcome of a group of patients who underwent an EPS because of abnormal noninvasive testing. Of 305 consecutive patients admitted to our institution after myocardial infarction, 67 (22%) were eligible for EPS because of the presence of ≥ 2 of the following noninvasive risk markers: Lown 4A-B ventricular arrhythmias at Holter monitoring, presence of ventricular late potentials at signal-averaged ECG, and depressed left ventricular ejection fraction (LVEF<0.40) at echocardiographic evaluation. EPS was performed in 47 of 67 (70%) eligible patients (mean age 58 ± 7 years, male gender 89%, anterior myocardial infarction 66%, thrombolysis treatment 41%, LVEF < 0.40 77%, presence of ventricular late potentials 68%, Lown 4A-B 70%) and was considered positive when sustained monomorphic VT was induced. During a follow-up of 9.5 ± 2.8 years, we observed 12 cardiac deaths (27%, sudden death in 3 cases) and 7 non cardiac deaths (16%); 5 deaths for unknown causes (11%) also occurred, 3 (6%) patients were lost at follow-up, non fatal sustained ventricular tachyarrhythmias occurred in 7 pts (16%). The analysis was performed in 39 patients with known cause of death. At univariate analysis we found that inducibility of sustained monomorphic VT was significantly different among patients with and without cardiac death as in patients with and without arrhythmic events (67% vs 26%, p = 0.02; 90% vs 24%, p = 0.001). At multivariate Cox regression analysis only LVEF manteined a significant prognostic power. No significant relationship was found between EPS result and all cause mortality. In conclusion, we report that inducible sustained monomorphic VT 1 month after a MI can suggest a poor cardiac prognosis in patients with high arrhythmic non-invasive risk profile, but in long-term follow-up only LVEF may be considered a significant predictor of adverse outcome.

1106-254 **Postmortem Cardiac Channel Genetic Testing in Autopsy Negative Sudden Unexplained Death: a Molecular Autopsy of 49 Medical Examiner/Coroner's Cases**

David J. Tester, Michael J. Ackerman, Mayo Clinic College of Medicine, Rochester, MN

Background: Potentially heritable arrhythmia syndromes may account for a significant number of autopsy negative, sudden unexplained deaths (SUD). Here, postmortem genetic testing (molecular autopsy) of the 5 cardiac channel genes implicated in

congenital long QT syndrome (LQTS) was performed in a cohort of medical examiner referred cases of SUD.
Methods: From September 1998 to March 2004, 49 cases of SUD (30 males, 13 with family history of syncope, cardiac arrest or sudden cardiac death, average age at death, 14 ± 11 years) were referred by Medical Examiners/Coroners to Mayo Clinic's Sudden Death Genomics Laboratory for a cardiac channel molecular autopsy. Comprehensive mutational analysis of all 60 protein-encoding exons of *KCNQ1* (LQT1), *KCNH2* (LQT2), *SCN5A* (LQT3), *KCNE1* (LQT5), and *KCNE2* (LQT6) was performed using DHPLC and direct DNA sequencing on genomic DNA extracted from decedent tissue.
Results: Eight putative LQTS-associated missense mutations (5 novel) were discovered in 8 SUD cases (16%, 6 females, average age at death = 18.5 ± 11 years). The activities at the time of SUD included sleep (4), exertion (2), auditory arousal (1), and undetermined (1). The mutations: L191fs/90-KCNQ1, G269S-KCNQ1, A302V-KCNQ1, W379R-KCNQ1, G584S-KCNQ1, R582fs/11-KCNH2, L799/sp-KCNH2, and I1768V-SCN5A, involved non-conservative amino acid substitutions in highly conserved residues across species. Each mutation was absent in over 1500 reference alleles. Expansion of decedent pedigrees is underway to delineate familial versus spontaneous germline transmission.
Conclusions: This study represents the largest molecular autopsy series of SUD. Here, 16% have a putative LQTS-associated mutation. Combined with our previous identification of 7 putative CPVT1-associated mutations involving the *RyR2*-encoded calcium release channel, we have provided molecular evidence for an underlying cardiac channelopathy as the likely cause and a fatal ventricular arrhythmia as the presumed manner of death in nearly one third of SUD cases. Postmortem cardiac channel genetic testing should be considered as a standard part of the evaluation of autopsy negative, sudden unexplained death.

1106-255 Cardiac Event Rate During Childbearing Years in Women With Long QT Syndrome

G. Michael Vincent, Xiaolin Xue, Li Zhang, LDS Hospital, Salt Lake City, UT

Background: Cardiac event (CE) rates during the pregnant, post-partum, and pregnancy unrelated (not pregnant or post-partum) periods in women with Long QT syndrome (LQTS) are not well defined, but an increased rate post-partum has been suggested.
Methods: CEs during these periods were compared in 252 child- bearing women with 739 pregnancies:101 LQT1 (16 *KCNQ1* mutations), 46 LQT2 (22 *KCNH2* mutations), 2 LQT3 (2 *SCN5A* mutations), 1 *KCNQ1+KCNH2,* and 102 ungenotyped women with definitive phenotype, from 119 families. Our 31 year old LQTS database is unique in that many of our pedigrees have been extensively expanded and then used to direct aggressive, prospective, screening of extended family members for LQTS. This has allowed identification of many asymptomatic and/or pre-symptomatic adults and children who otherwise would not come to medical attention. Post-partum was defined as the 40 weeks after delivery.
Results: CE rates during the three time periods for all 252 patients are shown in the table. ( ) show # of patients.

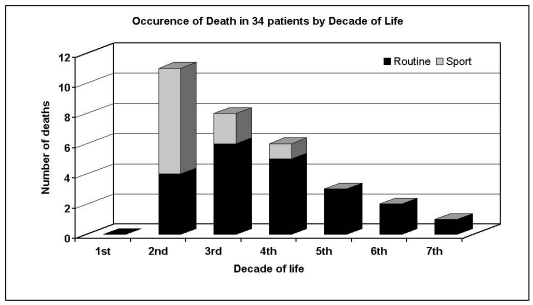
Time period	Syncope	Cardiac Arrest	Sudden Death	Total CE
Pregnancy unrelated	19.4% (49)	4.4 % (11)	4.4 % (11)	20.6 % (52)
Pregnant	2.8 % (7)	0.4% (1)	0	3.2% (8)
Post-partum	1.2 % (3)	0.8% (2)	0	2 % (5)

CE rates were also compared in genotyped LQT1 vs LQT2 patients to examine for genotype specific differences: pregnancy unrelated CE occurred in 16.8% vs 43%; pregnancy 4% vs 4%; and post-partum 1% vs 4%, respectively.
Conclusions: CE in childbearing years occur primarily in the pregnancy unrelated period. CE rates during pregnancy and post-partum periods are much less frequent. The data also confirm prior observations that LQT2 women have more CE in the childbearing age range than do LQT1 women.

1106-256 Sudden Cardiac Death in Patients with Arrhythmogenic Right Ventricular Dysplasia: A Series of 31 Cases from United States

Darshan Dalal, Kalpana Prakasa, Chandra Bomma, Jun Dong, Khurram Nasir, Crystal Tichnell, Cynthia James, Hugh Calkins, Johns Hopkins University School of Medicine, Baltimore, MD

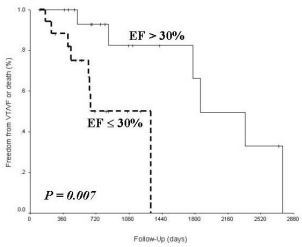
Background: Arrhythmogenic right ventricular dysplasia (ARVD) is an important cause of sudden death (SCD) in young individuals. The purpose of our study was to examine the demographics, circumstances and clinical course of a series of ARVD patients from the United States who were diagnosed with ARVD on autopsy.
Methods: Our study population was comprised of 31 patients who died suddenly and in whom ARVD was present at autopsy. The medical history of each patient and circumstances of death was determined.
Results: There were 31 patients (16 male) with a mean age at death of 29±15 years. Symptoms prior to experiencing SCD were present in 11 patients (palpitations in 2, syncope in 8, near syncope in 1). In 20 patients, SCD was the first manifestation of ARVD. Among the15 women in this series, one experienced SCD during pregnancy and one experienced her first symptoms during pregnancy. The SCDs occurred during exercise in 9 patients (29%). SCD was most common between the 2nd and 4th decades of life. Death related to exercise was only observed in individuals who died before 40 years of age (figure).
Conclusions: The results of this study demonstrate that the majority of patients who experience sudden cardiac death from ARVD are young adults and do not have warning symptoms prior to SCD. Most deaths occur during routine activity. The probable association between SCD and pregnancy detected in this study needs further investigation and may have important implications for management of ARVD patients contemplating pregnancy.



1106-257 Can We Identify High-risk Patients With Non-ischemic Cardiomyopathy Who Present With Syncope?

Suneet Mittal, Amit B. Guttigoli, Brian Wilner, Kenneth M. Stein, Steven M. Markowitz, Sei Iwai, Bindi K. Shah, Ravi K. Yarlagadda, Bruce B. Lerman, Cornell University Medical Center, New York, NY

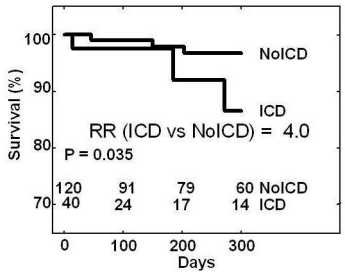
Background: Based on recently published data, ICD implantation has been advocated in all patients (pts) with underlying non-ischemic cardiomyopathy who present with syncope, irrespective of the findings at electrophysiologic (EP) testing. However, it would be clinically useful to identify pts who benefit most from this strategy. Therefore, we sought to identify long-term predictors of arrhythmic events and/or death in these pts.
Methods: We identified 35 consecutive pts (20 M, 63 ± 15 yrs, EF 29 ± 9 %) with non-ischemic cardiomyopathy (LVEF ≤ 45%) who underwent ICD implant for management of unexplained syncope. All pts underwent EP testing; however, an ICD was implanted irrespective of inducibility of VT. Pts were followed at 3-6 mo intervals and EGMs from their ICDs were retrieved.
Results: During a follow-up of 905 ± 672 days, 11 pts received appropriate ICD therapy [monomorphic VT (n=8) or VF (n=3)] and 6 pts died. There was no difference in age, gender, medications, NYHA class, QRS duration, or inducibility of VT between pts who did and did not meet the combined end-point of arrhythmia (VT/VF) or death. However, arrhythmia-free survival was significantly less likely in pts with a LVEF ≤30% (n=17, dashed line) than in pts with a LVEF >30% (n=18, solid line, p=0.007, Figure). The 1 and 2 year arrhythmia-free survival rate was 100% and 92% for pts with a LVEF > 30%, but only 88% and 50% for pts with a LVEF ≤ 30% .
Conclusions: Patients with a non-ischemic cardiomyopathy and history of syncope have good overall survival when treated with an ICD. However, our data suggest that in this patient population, an EF ≤30% identifies pts who derive the greatest benefit from ICD implantation.



1106-258 Prophylactic Defibrillator Therapy is Associated With Increased Mortality in Microvolt T-Wave Alternans Negative Patients with Ischemic Cardiomyopathy

Theodore Chow, Richard Cohen, Cheryl Bartone, Edward J. Schloss, Theodore Waller, Terri Booth, Eugene Chung, Santosh Menon, Dean Kereiakes, Ohio Heart Health Center, Cincinnati, OH

Background: Since defibrillator (ICD) therapy is associated with some risk, including worsened heart failure and inappropriate shocks, prophylactic implantation in low risk patients could potentially increase mortality. Microvolt T-wave alternans (MTWA) is a test with excellent negative predictive value for sudden death risk. We evaluated the hypothesis that ICD therapy would increase mortality in MTWA negative patients.
Methods: Cardiology outpatients with LVEF≤ 40% within a large practice underwhent MTWA testing (primarily by treadmill exercise). MTWA tests were interpreted according to published criteria. Treatment strategy and ICD programming were per physician discretion. All patients were maintained in a prospective registry with follow-up by telephone contact and chart review. Subgroup analysis on patients with coronary diseasae (CAD) and LVEF ≤ 30% was performed.
Results: 413 patients with CAD and LVEF ≤ 30% (average = 25%±5%) were followed for a mean of 362 days; 40/160 MTWA negative patients received ICDs. Kaplain-Meier analysis for freedom from death according to ICD treatment status in MTWA negative patients was performed (Figure). Survival at 300 days was 0.866 for ICD patients and 0.966 for non-ICD patients (relative risk=4.0, p=0.035).
Conclusions: Prophylactic ICD treatment of MTWA negative patients with CAD and EF≤30% is associated with worse survival. Whether bradycardia pacing contributes to this outcome requires further study.



1106-259 **Arrhythmia Or Thrombosis: What is the Dominant Mechanism of Sudden Cardiac Death Risk Conferred by LVH?**

Celia Dervan, Eric C. Stecker, Carmen Miu, Kalpana Narapasetty, Catherine Vickers, Justin Waltz, Benjamin T. John, Karen Gunson, John H. McAnulty, Jr., Sumeet S. Chugh, Oregon Health and Science University, Portland, OR

Background: The Framingham Heart Study reported an independent association between left ventricular hypertrophy (LVH) and sudden cardiac death (SCD), but due to the absence of autopsy data, mechanisms of the terminal event are continually debated. We performed detailed postmortem examinations to evaluate the pathophysiology of SCD in subjects with LVH in an ongoing, community-based study.
Methods: The Oregon Sudden Unexplained Death Study (Ore-SUDS) is a prospective, multiple-source population-based study of SCD among all residents of Multnomah County OR (Pop. 660,486). SCD was defined as unexpected death within 1 hr of symptoms (witnessed) or within 24 hrs of being observed healthy (un-witnessed). In addition, subjects with known, non-cardiac causes of death were excluded. During 2002 and 2003, findings in 32 SCD cases age 30-60 yrs (mean age 47 y; 78% male) that underwent detailed postmortem examination were compared with 29 age and sex-matched controls that suffered non-cardiac, unnatural death (mean age 44 y, 79% male ; p=NS vs. cases).
Results: LVH was significantly more common in cases vs. controls (53 vs. 14%, p<0.01) with a higher body mass index in cases (33 vs. 28, p<0.01). Overall, 75% of cases had significant coronary artery disease (CAD) vs. 28% of controls (p<0.05). Among cases with LVH, evidence of acute myocardial infarction (coronary thrombosis or fresh infarct) was identified only in 3 cases (18%). The remainder had significant chronic CAD (n=10), other diagnoses (n=2; arrhythmogenic right ventricular dysplasia, pulmonary valve stenosis) and otherwise normal heart (n=2). Among controls with LVH, 3 subjects had additional cardiac abnormalities (CAD n=2; mitral valve prosthesis n=1).
Conclusions: These data confirm the strong association between LVH and SCD and suggest that the mechanism of the terminal event is significantly more likely to be fatal arrhythmia (82%) vs. acute coronary thrombosis (18%).

1106-260 **Earlier Peak Systolic Strains Analyzed By Tagged MRI Are Related To Inducibility For Ventricular Tachycardia In Patients With Ischemic Cardiomyopathy**

Boaz D. Rosen, Katherine C. Wu, Caterina Silva, Veronica Fernandes, Khurram Nasir, Ronald Berger, Joao AC Lima, Johns Hopkins Hospital, Baltimore, MD

Background: Sudden cardiac death due to ventricular arrhythmias is common in patients with ischemic cardiomyopathy (ICM). Existing non-invasive parameters cannot identify high risk patients reliably. We used myocardial tissue tagging to examine differences in regional myocardial deformation and relate them to inducibility for arrhythmia by electrophysiologic study (EPS).
Methods: 16 patients with ICM underwent tagged and contrast enhanced MRI studies to analyze regional LV function and infarction areas, respectively. All patients were recruited as part of the Johns Hopkins Reynolds project. Time to peak systolic circumferential strain (Ecc) was analyzed in 12 regions of short axis images. Segments were grouped according to distance from the infracted region defined by delayed hyperenhancement into remote, adjacent and infarcted regions. All patients underwent invasive (n=3) or non-invasive (n=13) EPS and those inducible for monomorphic VT were considered positive. Relationship between time to peak systolic strain and inducibility was studied.
Results: 7 patients were inducible. Both extent of infarction and ejection fraction were similar between groups. Importantly, mechanical activation expressed as time to peak systolic Ecc, was different between inducible and noninducible patients. Average time to peak Ecc was earlier in inducible compared to noninducible patients (304.3±117.1 versus 381.7±188.5 ms, p<0.001) but only reached statistical significance in the infarct and remote regions (303.8±118.6 vs 392.1±184.6, p=0.02, and 303.7±121.5 vs 376.7±196.3, p=0.03 in inducible and noninducible patients, respectively). In 9 out of 12 regions, the time to peak Ecc was greater than 360 ms in noninducible patients, while in inducible patients it was less than 360ms in *all* regions (p<0.0001 by Fisher exact test).
Conclusions: Earlier mechanical activation determined by peak systolic strain in patients with ischemic cardiomyopathy is related to inducibility for ventricular tachycardia and may help in understanding the anatomic substrate that underlies monomorphic reentry in these patients.

1106-261 **Myocardial Scar Morphology as Determined by Magnetic Resonance Imaging Identifies Substrate for Ventricular Tachycardia**

Mark W. Kolasa, Carey O'Bryan, Richard Krasuski, Javier Roman-Gonzalez, Wilford Hall Medical Center, Lackland AFB, TX, Brooke Army Medical Center, San Antonio, TX

Background: Over 300,000 patients die annually due to sudden cardiac death. Left ventricular (LV) dysfunction has been identified as a principle risk factor for malignant arrhythmias. An electrophysiology study (EPS) using programmed ventricular stimulation is an invasive method of risk stratification in patients with reduced LV function. Contrast enhanced cardiac magnetic resonance imaging (CMR) has been demonstrated to be an accurate method of detecting and characterizing myocardial scar. The spatial resolution provided by CMR allows clear delineation of scar location and thickness. We hypothesized that the extent of transmural scar and total scar burden would be predictive of inducible monomorphic ventricular tachycardia (MVT) at EPS.
Methods: Patients undergoing implantation of an Implantable Cardioverter Defibrillator (ICD) for primary or secondary prevention of sudden cardiac death, according to current national guidelines, underwent contrast enhanced CMR. Myocardial scar was identified and characterized by location and thickness in the left ventricle. Additionally, scar burden was measured volumetrically. At the time of ICD implantation, patients underwent EPS for ventricular arrhythmia. The inducibility of MVT was compared to scar thickness and scar burden.
Results: CMR was completed on 18 patients prior to EPS. MVT was induced in 10 patients. The mean ages of patients with and without inducible MVT were 69.2 +/- 7.3 and 64.0 +/- 9.6 years respectively (p=0.23). The mean ejection fractions of the patients with and without inducible MVT were 27.0% +/- 2.9% and 27.3% +/- 6.1% respectively (p=0.89). In patients with inducible MVT, 29.7% +/- 21.6% of LV segments with scar had a scar thickness >75%, compared to 2.6% +/- 4.3% in patients who were noninducible (p=.02). Volumetric scar burden was not associated with increased inducibility.
Conclusion: In areas of scar, the number of left ventricular myocardial segments with thickness >75% as identified by contrast enhanced CMR is predictive of inducible MVT at EPS. In a population of patients at risk for ventricular arrhythmias, CMR may be an effective, non-invasive method of risk stratification.

1106-262 **The Demonstration of Ventricular Muscle Extensions into the Pulmonary Artery and Aorta Beyond the Semilunar Valves**

Can Hasdemir, Safiye Aktas, Figen Gokmen, Ekin O. Aktas, Aytac Kocak, Okan Kok, Yasemin Turan, Cem Ulucan, Muge Ildizli, Oner Ozdogan, Meral Kayikcioglu, Levent H. Can, Serdar Payzın, Ege University School of Medicine, Izmir, Turkey, Behcet Uz Children Research Hospital, Izmir, Turkey

BACKGROUND: It has been shown that idiopathic ventricular tachycardia may originate from the aortic and pulmonary root. Therefore, we have studied tissue structure for ventricular muscle extensions into the pulmonary artery and aorta beyond the semilunar valves.
METHODS: 50 human hearts (mean age 44±17 years, male/female: 40/10) were examined and the extent of ventricular musculature beyond the semilunar valves studied. Tissue structure was assessed in paraffin-embedded tissue using Gomori trichrome staining in serial sections.
RESULTS: Ventricular muscle was seen extending into the pulmonary artery beyond the pulmonary valve in 5/50 cases (10%). This sleeve of ventricular muscle extended for 3±1.7 mm (range 2-6 mm) into the pulmonary artery. Ventricular muscle was seen extending into the aorta beyond the aortic valve in 5/50 cases (10%). This sleeve of ventricular muscle extended for 4.4±1.7 mm (range 3-7 mm) into the aorta. While extensions into the pulmonary artery were circumferential, muscular extensions into the aorta primarily occured in relation to the left and non-coronary cusp.
CONCLUSIONS: Sleeves of ventricular muscle extend beyond the semilunar valves into the aorta and pulmonar artery. The role of these ventricular muscle extensions as the potential substrate for idiopathic ventricular tachycardia needs to be clarified by further studies.

POSTER SESSION

1107 Clinical Aspects of Defibrillation

Monday, March 07, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 1:30 p.m.-2:30 p.m.

1107-247 **The Impact of Catecholamines on the Defibrillation Threshold of Patients Receiving Carvedilol**

Michael White, Brian F. Mcbride, Danette Guertin, Bokyung Min, Christopher Clyne, Jeffrey Kluger, Hartford Hospital, Hartford, CT, University of Connecticut, Storrs, CT

Background: Defibrillation threshold (DFT) is the minimum energy required to successfully terminate ventricular fibrillation. In a previous study in patients with an implantable cardioverter-defibrillator (ICD), we found that norepinephrine lowered DFT regardless of baseline treatment with cardioselective beta-blockers or no beta-blockade (BB). Epinephrine reduced the DFT in those receiving cardioselective BB but increased it among those without BB. We hypothesized that alpha-1 receptor stimulation decreases DFT and attenuates the adverse effect of epinephrine on DFT in beta blocker treated patients, but that patients treated by the beta-nonselective and alpha-1 blocker carvedilol may respond differently.

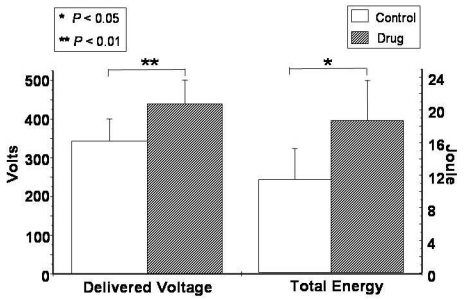
Methods: In this double-blind study, DFT was determined by step-down method (Baseline DFT) and then patients (n=27, 28.7mg of carvedilol/day, 67.3 years, 70.0% male, 19% LVEF) were randomized to a seven-minute infusion of norepinephrine (2mcg/min), epinephrine (2mcg/min), or placebo. Following study infusion, DFT testing was repeated (Experimental DFT).
Results: Following administration of norepinephrine, epinephrine, or placebo, no intragroup or intergroup DFT differences were observed (Table).
Conclusions: Carvedilol prevents alterations in DFT produced by stress levels of catecholamines. This includes negativing the negative effects of epinephrine and positive effects of norepinephrine on DFT.

	Baseline DFT	Experimental DFT	Intragroup P-value
Norepinephrine (n=9)	9.4±4.6	11.1±7.8	P=0.589
Epinephrine (n=9)	10.6±5.3	9.8±6.3	P=0.779
Placebo (n=9)	11.1±7.0	8.5±4.2	P=0.349
ANOVA Intergroup P-Value	P=0.812	P=0.681	

1107-248 Sildenafil Citrate Markedly Increases Defibrillation Threshold in Swine

Krekwit Shinlapawittayatorn, Rattapong Sangnoon, Siriporn Chattipakorn, Wanna Suriyasataporn, Nipon Chattipakorn, Chiang Mai University, Chiang Mai, Thailand

Background: Sildenafil citrate is commonly used to treat erectile dysfunction. Although a growing number of reports have related this drug to the cause of fatal arrhythmia and sudden cardiac death, its effect on defibrillation efficacy has not been investigated. The aim of the present study was to test the hypothesis that Sildenafil citrate increases the shock strength required to successfully defibrillate during ventricular fibrillation (VF).
Methods and Results: Six pigs (20-30 kg) were used in this study. In each pig, the defibrillation thredshold (DFT) was determined at the beginning of the study using a three-reversal up/down protocol. Each shock (RV-SVC, biphasic) was delivered after 10 seconds of VF. After a control DFT was obtained, a solution contained 100 mg Sildenafil citrate was injected intravenously at the rate of 2 cc/min over 50 minutes. The DFT (drug-DFT) was determined again after the drug administration. The drug-DFT (478 ± 66 V, 19 ± 5 J) was significantly (P<0.003 and P<0.01 respectively) higher than the control DFT (371 ± 60 V, 12 ± 4 J). There was no significant change in the heart rate as well as the systolic blood pressure before and after drug infusion. Sildenafil citrate increased the DFT ~29 % by leading-edge voltage, and ~58 % by total energy. **Conclusion:** Sildenafil citrate, a cGMP-specific PDE5 inhibitor, significantly increased the DFT. This finding indicates that VF occurring during Sildenafil treatment will require a much stronger shock to successfully defibrillate.



1107-249 Influence of Race and Gender on the Use of Implantable Defibrillator Therapy among Medicare Beneficiaries

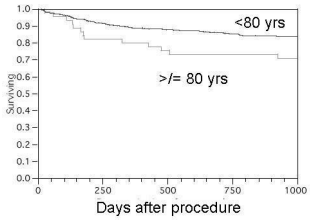
Andre J. Gauri, Andrew Davis, Thomas Hong, Aseem Desai, Martin C. Burke, Bradley P. Knight, University of Chicago Hospitals, Chicago, IL

Background: Implantable defibrillator (ICD) is underutilized for the primary prevention of sudden cardiac death in patients with an ischemic cardiomyopathy (ICM) despite the results of randomized trials that support its use. Other studies have shown that the utilization of cardiac procedures is lower in women and black patients. The purpose of this study was to determine if there is a gender or racial bias in the use of ICD therapy.
Methods: 1,889,966 Medicare patients hospitalized in the United States during the year 2002 with a diagnosis of coronary artery disease, prior myocardial infarction, or congestive heart failure were identified from the Center for Medicare and Medicaid Services database. Using combinations of ICD-9-CM codes, patients with an ICM were identified. From this group, patients who underwent ICD implantation during the same year were identified. The demographics of the patients with an ICM were compared to those of the ICD recipients.
Results: 132,565 patients (7%) were identified as having an ICM. 10,370 of these potential ICD candidates (8%) underwent ICD implantation. The ICD recipients differed significantly from the overall group of patients with an ICM on the basis of both gender (16% vs. 35%, women; p<0.001) and race (5.5% vs. 8.0%, black; p<0.001).
Conclusions: Women and black patients may be underrepresented in the elderly ICD population. Further exploration of gender and racial barriers to appropriate ICD use is indicated.

1107-250 Longevity in Octogenarians Following Cardiac Resynchronization Therapy: Is it worth it?

Jennifer E. Cummings, John L. Drago, William A. Belden, Patrick J. Tchou, Mina K. Chung, Cleveland Clinic Foundation, Cleveland, OH

As indications for device therapies increase and left ventricular lead implantation becomes more commonplace, the use of cardiac resynchronization is increasing rapidly. With aging of the population, a larger number of patients over the age of 80 are receiving such devices.
Methods: After new biventricular device implantation in 630 patients from 2/97-5/04, survival status was assessed by the Social Security Death Index. Univariate, multivariate, and survival analyses were performed to assess survival and predictors of mortality in octogenarians compared to younger patients.
Results: Over a follow-up period of 20.9±15.9 mos, 114 (18.1%) patients died. Patients over 80 years of age were lower in weight (72.4±10.4, 83.7±19.2, p<0.001) and had shorter procedures. Although mortality was significantly associated with higher age, median survival in pts ≥80 years was >4 yrs. Interestingly, those patients ≥ 80 years of age did not appear to have any additional benefit in survival with the use of a biventricular defibrillation device as compared to a biventricular pacing device.
Conclusions: Although older age is significantly associated with higher mortality after CRT implantation, median survival was over 4 years in patients ≥ 80 years old. Use of an internal defibrillator CRT did not appear to improve survival when compared to those receiving CRT alone. These findings support proceeding with CRT implantation with or without defibrillation capacity in octogenarians with appropriate indications.

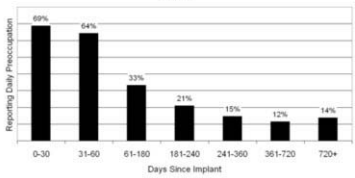


1107-251 Psychosocial Adjustment and Post-Implant Attenuation of ICD Preoccupation

Howard S. Farkas, Rena Binter, Julie Schmittdiel, Jane Kruse, Alan H. Kadish, Jeffrey J. Goldberger, Northwestern University Feinberg School of Medicine, Chicago, IL

Background: Implantation of an ICD may provoke patient anxiety. One measure of this is device preoccupation. The purpose of this study is to determine the time course for adjustment to an implanted ICD using preoccupation as the criterion.
Methods: A cross-sectional study of all patients followed in our ICD clinic was done over a 12-month period. During routine follow-up appointments, patients rated frequency of ICD-related thoughts. Adjustment was defined as less than daily frequency.
Results: 416 patients (329 male, age 62.4 ± 14.8) were interviewed, with a total of 864 observations. Up to 60 days post-implant, 66% of respondents reported at least daily ICD-related thoughts (Fig.1). After 2 months, this dropped to 33%, and to 21% after 6 months. Beyond 8 months post-implant, fewer than 15% reported thinking about their device daily. By ANOVA, there was a significant time-related reduction in ICD preoccupation (p<.001) with a greater degree of preoccupation in women (p=.02) and patients younger than age 45 (p=.02).
Conclusion: Adjustment to an ICD normally takes two to six months. Notably, up to 15% of ICD patients report persistent ICD preoccupation even beyond the first year. In the first year, males and patients over age 45 adjust better than females and younger patients. Information about the normal time course for adjustment to the ICD may allay patient anxiety and enhance ICD acceptance. It can also help to identify patients who have difficulty adjusting and may benefit from more intensive support.

Figure 1



1107-252 Elevated B-type Natriuretic Peptide Is Associated With Ventricular Tachyarrhythmic Events Determined By ICD Interrogation In Congestive Heart Failure Patients

Roland Klingenberg, Christian Zugck, Ruediger Becker, Dieter Schellberg, Robert Kell, Andrew Remppis, Wolfgang Schoels, Thomas J. Dengler, University Hospital Heidelberg, Heidelberg, Germany

Background: To evaluate whether B-type natriuretic peptide (NT-proBNP) is associated with ventricular tachyarrhythmic events as a surrogate of sudden cardiac death in congestive heart failure (CHF) patients and to determine its potential for predicting further events.

Methods: In this retrospective analysis 51 CHF patients (NYHA I-III) with ejection fraction < 40% (63% dilated and 37% ischemic cardiomyopathy) and prior ICD-implantation for primary or secondary prevention of malignant ventricular tachyarrhythmia presenting to our institution from 1995-2002 were analyzed. The main outcome measures were the association of NT-proBNP with ventricular tachyarrhythmic events assessed by ICD interrogation and tachyarrhythmia-free survival according to NT-proBNP stratification.
Results: Ventricular tachyarrhythmia was detected in 33 % of patients at first visit. ROC analysis for the diagnosis of ventricular tachyarrhythmia was performed, yielding an AUC of 0.81 for a NT-proBNP level of 604 ng/l with a sensitivity of 66.7 %, specificity 91.1 %, negative predictive value 0.91 and a positive predictive value of 0.8. ICD interrogation was performed at 6 visits (median) during a mean follow-up (SD) of 2.07 (1.66) years. Tachyarrhythmia-free survival after one year was significantly worse (p = 0.003) in patients with elevated NT-proBNP (optimized cut-off level of ≥ 675 ng/l). Univariate analysis identified LVEF (p = 0.002), NT-proBNP (p = 0.007), NHYA class (p = 0.025) and NSVT (p = 0.049) as significant predictors of ventricular tachyarrhythmia. Multivariate pairwise analysis identified NT-proBNP as an independent predictor of ventricular tachyarrhythmia.
Conclusions: Elevated NT-proBNP adequately detects and predicts episodes of documented ventricular tachyarrhythmia in CHF patients with an ICD. Prospective evaluation of NT-proBNP to identify candidate CHF patients for ICD implantation appears appropriate.

1107-270 Successful Reimplantation of Pacemaker/Defibrillator Systems following Complete Explantation for Infection

George A. Yesenosky, Sweta Chandela, Aditya Mehra, Scott Sinner, Steven P. Kutalek, Drexel University College of Medicine, Philadelphia, PA

BACKGROUND: Specific guidelines do not exist for managing pacemaker (PM) and defibrillator (ICD) system infections, often life threatening. There is no consensus for antibiotic duration, value of presenting symptoms, or the role of comorbid conditions.
METHODS: We present our experience with PM/ICD infections with regard to clinical presentation, culprit pathogens, effect of comorbidities, and management. Demographics and clinical presentation of patients (pts) referred to our center for extraction are also reviewed.
RESULTS: Of 250 pts with PM/ICD infections, 241 had extraction of the entire device system (8 retained remnants, one with epicardial leads). There were 186 males. Device infection from implant occurred Early (0-28 days) =6%, Late (29-364 days) =22%, or Delayed (≥365 days) =72%. Surgical device manipulation after first implant occurred in 95 pts. Comorbidity included diabetes - 84; dialysis - 19; ethanol abuse - 9; systemic steroids - 9; and IV drug abuse - 1. Systemic signs included fever/chills - 102; septic shock - 17; and lead vegetation - 59. Local signs included skin erosion - 95; pain - 78; erythema - 87; and pocket swelling - 89. Cultures were positive in blood in 112 pts and in wounds in 161 pts.
The most common organism was Staphylococcus in blood (35%) and wounds (59%). Enterococcus, Candida, Group B Streptococci, Eschrichia coli, Pseudomonas, Micrococcus, Mycobacterium, and polymicrobials infected 8% of blood cultures. Polymicrobials (15%), Propioibacterium, Pseudomonas, Enterococcus, Micrococcus, Eschrichia coli, Proteus, and Klebsiella (each ≤ 3%) infected wounds. Citrobacter, Peptostreptomagnus, Enterobacter, Mycobacterium, Serratia and Streptococcus infected 3% of wounds. The most common antibiotics were vancomycin and cephalosporins.
Treatment included contralateral reimplantation, after clearing blood cultures and vegetations, and IV antibiotics through reimplant; reinfection rate was < 1%.
CONCLUSIONS: Reimplantation of PM/ICDs following local or systemic infection is highly successful, with minimal recurrence, using aggressive complete system explant and IV antibiotics. Comorbidities have no adverse effect on long-term prognosis.

1107-271 Lower Current Density Ventricular Defibrillation Thresholds With Dual Pathway Rectilinear Biphasic Shocks

Mark J. Niebauer, John Lof, Elizabeth Stolze, Sherry Westphal, Gretchen Andersen, Allen Missoi, Mike Petrocchi, James Brewer, University of Nebraska Medical Center, Omaha, NE

External ventricular defibrillation using the rectilinear biphasic waveform (RBW) is effective, and requires less energy than the monophasic damped sine waveform (DSW). Earlier studies found that two dual pathway (DP), shocks using the DSW, improved defibrillation effectiveness compared to single pathway shocks. Shocks delivered to the heart using 2 orthogonally positioned electrodes could more effectively stimulate a larger amount of the ventricle, since stimulation thresholds are lower for electric fields oriented in the long axis of the myocyte compared to the short axis.
Methods: Using 12 anesthetized pigs, 34.7± 2.3 kg, we tested the single RBW and 4 different DP-RBW positions for defibrillation efficacy, with DP shocks delivered both simultaneously (Sim) and sequentially (Seq). We used a "3-reversal" defibrillation threshold value, calculated from the average of 4 shock values above and below the point of success. The threshold energies and the calculated intrathoracic current densities (CD) were obtained for each of the shock positions. The results were compared to the single anterior-posterior RBW shock using the paired t-test.
Results: See means and SD in Table where * p< 0.05.
Conclusion: While total selected energies at threshold from DP-RBW shocks are not significantly different from the single pathway RBW shock, we found that the CD of the DP-RBW shocks in position 3 and the sequentially delivered shocks in Positions 1 and 2 were significantly lower than the single RBW shock vector.

	Single RBW	Position 1	Position 2	Position 3	Position 4
Energy Sim (J)	56.6 ± 19.3	71.5 ± 27.8	73.4 ± 34.0	48.1 ± 24.7	74.4 ± 22.1
Energy Seq (J)	----------	53.8 ± 26.	54.2 ± 19.0	53.1 ± 19.3	67.8 ± 20.4
CD Sim (mA/cm2)	94.3 ± 17.7	68.8 ± 16.8	70.4 ± 22.1	59.0 ± 15.2*	71.8 ± 11.2
CD Seq (mA/cm2)	----------	60.1 ±15.9*	63.8 ±12.5*	62.8 ± 10.0*	68.6 ± 11.3

1107-272 Adoption of MADIT II Guidelines by Private Health Insurers

Kenneth Martin Stein, Julio A. Casillas, Weill Medical College of Cornell University, New York, NY, Guidant CRM, Saint Paul, MN

Background: In March 2002, the MADIT II trial was published, showing a statistically significant survival benefit to prophylactic ICD implantation in pts with an EF ≤ 30% after myocardial infarction. In August 2003, CMS issued a National Coverage Decision (NCD) including MADIT II criteria albeit with an additional requirement that patients have a QRS width > 120 ms. The present study was designed to examine the guidelines that large private health insurers use when considering coverage for MADIT II indications.
Methods: We surveyed 11 large national and regional private payer groups to identify specific coverage guidelines for MADIT II, how guidelines or policies were set, and what specific or clinical resources payers relied upon to set them.
Results: The 11 private groups represent 152 plans covering approximately 152 million lives. All plans surveyed indicated adoption of some degree of coverage for MADIT II indications, but only 43% of plans published their guidelines. 143/152 plans representing 147 million lives indicated that they would cover prophylactic ICD implantation for pts with EF ≤ 30% following myocardial infarction. Only 9/152 plans (6%), covering 5.2 million lives (3% of covered lives) added a CMS-type QRS restriction to their coverage policy. No plan that had previously published a MADIT II coverage policy that reflected clinical indications, restricted coverage following publication of the CMS NCD. Finally, in contrast to CMS, many private payers assert that they will consider expanded coverage based on medical necessity on an individual basis, regardless of influencing standards, to allow providers the clinical discretion to treat patients.
Conclusion: The private insurance market has adopted MADIT II clinical guidelines widely. In this context, the CMS NCD had limited influence on private payer coverage determinations. The wide discrepancy between private and government payment policies for prophylactic ICD implantation raises the concern that patients and implanting physicians in the US must now contend with a de facto "two-tier" system when considering prophylactic ICD implantation.

POSTER SESSION

1108 Noninvasive Markers of Atrial Function

Monday, March 07, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 1:30 p.m.-2:30 p.m.

1108-267 Maintenance of Sinus Rhythm in Patients With Atrial Fibrillation Following Electrical Cardioversion Is Related to Reverse Electrical Remodeling of the Atrium

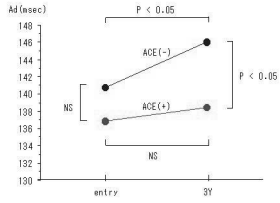
Nagib T. Chalfoun, David Harnick, Davendra Mehta, Elena Pe, J. Anthony Gomes, Mount Sinai Medical Center, New York, NY

BACKGROUND: The signal-averaged ECG of the P wave (SAPW), which is a measure of intra-atrial conduction, has been shown to be a non-invasive marker of the risk of developing atrial fibrillation (AF). We hypothesized that 1) atrial electrical reverse remodeling (AERM) occurs in patients who maintain sinus rhythm post cardioversion (CV) for persistent AF and 2) that AERM can be measured by changes in the SAPW parameters.
METHODS: To test this hypothesis, we prospectively enrolled 59 patients with persistent AF. SAPW parameters, including duration, root mean square voltage of the last 20/30/40 milliseconds, and total integral of the p wave were measured the day of CV if the patient was successfully cardioverted to SR, and repeated at 1 month in those who maintained SR. These SAPW parameters were compared to other baseline indices for the recurrence of AF, including age, gender, left ventricular function, AF duration, left ventricular hypertrophy, hypertension, history of myocardial infarction, diabetes, alcohol, hyperthyroidism, history of chest surgery, atrial size, presence at least moderate mitral valvular disease, and antiarrhythmic therapy post CV.
RESULTS: 55 patients had successful CV; 29% females, 71% males. Mean age was 61 ± 13 years. At 1 month, 18 (33%) maintained SR, whereas 37 (67%) returned to AF. The SAPW duration decreased significantly in those that remained in SR (159 ms ± 19 to 147 ms ± 19; p<0.0001). Of the parameters tested, only the duration of AF (p=0.04) and presence of left ventricular hypertrophy (p=0.0003) were significantly different in the patients who maintained SR versus those who reverted back to AF.
CONCLUSIONS: 1) This is the first non-invasive study that documents atrial electrical reverse remodeling in patients with atrial fibrillation who maintain sinus rhythm post cardioversion utilizing the SAPW. 2) Atrial electrical reverse remodeling is inversely related to the duration of atrial fibrillation and the presence of left ventricular hypertrophy.

1108-268 **The Effect of ACE Inhibitors on Atrial Electrical Remodeling in Patients With Congestive Heart Failure**

Shunsuke Tamaki, Naoyuki Misaki, Takahisa Yamada, Mitsutoshi Asai, Nobuhiko Makino, Hidetaka Kioka, Yasumasa Tsukamoto, Fumihiko Sano, Masaharu Masuda, Takaki Matsumoto, Masatake Fukunami, Osaka General Medical Center, Osaka, Japan

Background: Recent studies have shown that ACE inhibitors(ACEi) could reduce the risk of development of atrial fibrillation(AF) in patients with congestive heart failure(CHF). We sought to elucidate the electrophysiological mechanism from a viewpoint of atrial electrical remodeling, by use of P-wave signal-averaged ECG(P-SAE).
Methods: We studied 63 CHF patients in sinus rhythm without a history of AF, whose radionuclide left ventricular ejection fraction was < 40%. P-SAE was repeated before and three years after the entry, to measure the total filtered P wave duration(Ad) which might reflect the extent of fibrosis as previously reported.
Results: There were no differences in age, gender, left atrial dimension, or ejection fraction between patients with and without ACEi. At the entry, there was no significant difference in Ad between patients with and without ACEi(136.9±12.0 vs. 140.8±10.7 ms). However, three years after the entry, Ad in the patients with ACEi was significantly shorter than that of without(138.4±11.6 vs. 146.0±13.8 ms, P = 0.04). Ad prolonged significantly in the patients without ACEi(P = 0.04) but not in with ACEi. Incidentally, AF developed less frequently with than without ACEi during the follow-up period (8.5% vs. 25%, P = 0.077 by log-rank test).
Conclusion: Our data showed that ACEi could inhibit the prolongation of Ad. These results suggest that ACEi could possibly attenuate atrial remodeling(fibrosis) leading to AF substrate, resulting in suppression of the AF development in CHF.



1108-269 **Are Certain P Wave Abnormalities More Predictive of Cardiovascular or Pulmonary Causes of Death in Men?**

Amir Kaykha, Kenneth Desser, Jonathan Myers, Gregory Engel, Afshin Ghayoumi, Victor Froelicher, Stanford University/VA Palo Alto Health Care System, Palo Alto, CA, Banner Good Samaritan Medical Center/Carl T Hayden VA Medical Center, Phoenix, AZ

Background: While certain P wave morphologies have been associated with pulmonary disease (P-pulmonale) and atrial size (left atrial abnormality or P-mitrale), their relationship to specific cause of death has not been reported. Our objective was to evaluate the prognostic value of P wave morphology as a predictor of cardiovascular (CV) and pulmonary causes of death.
Methods: Analyses were performed on the first ECG digitally recorded on 46,917 consecutive patients at the Palo Alto Veterans Affairs Medical Center since 1987. Females and ECGs exhibiting paced rhythms, Wolf-Parkinson-White syndrome, atrial fibrillation and those in which the computer algorithm failed to detect the P wave were excluded, leaving 40,021 patients, with a mean age of 56 years. Using computerized algorithms, P wave amplitude in the inferior leads and P wave duration in 12 leads were measured. Left atrial abnormality and right atrial abnormality were defined by standardized computer criteria. The main outcome measures were pulmonary and CV mortality.
Results: During a mean follow-up of 6 years there were 3,421 CV and 1,217 pulmonary deaths. After adjusting for age and heart rate in a Cox regression model, P wave amplitude in the inferior leads was the strongest predictor of pulmonary death [Hazard Ratio 3.1, CI 2.3-4.0, p<0.0001 for an amplitude more than 2.5mm], outperforming all other ECG criteria for right atrial abnormality and right ventricular hypertrophy. However, P wave duration was inversely associated with pulmonary death. Conversely, P wave duration and the depth of P wave inversion in leads V1 and V2 were the strongest predictors of CV death [Hazard Ratio 1.9, CI 1.6-2.3, p<0.0001; for a P wave inversion deeper than 1 mm].
Conclusion: P wave amplitude is directly associated with pulmonary death but inversely associated with CV death while the converse is true for P wave duration. P wave amplitude in the inferior leads is the strongest independent predictor of pulmonary death while P wave duration significantly predicts CV death.

ORAL CONTRIBUTIONS

830 Mechanisms and Mapping of Supraventricular Tachycardia

Monday, March 07, 2005, 4:00 p.m.-5:30 p.m.
Orange County Convention Center, Room 232A

4:00 p.m.

830-3 **Combined Electroanatomic and Non-contact Mapping to Identify Fixed and Functional Conduction Block after the Atriopulmonary Fontan Procedure.**

Dominic J. Abrams, Mark J. Earley, Simon C. Sporton, Michael A. Gatzoulis, Michael J. Mullen, Janice A. Till, Saemus Cullen, John E. Deanfield, Richard J. Schilling, St. Bartholomew's Hospital, London, United Kingdom

Background: It has been proposed that atrial arrhythmia after the atriopulmonary Fontan (APF) procedure relates to fixed anatomical barriers and/or scar, suggesting that an empiric ablation strategy may be possible. We proposed that functional block may also play an important role in these arrhythmias and may relate to atrial structure and patient characteristics.
Methods: We studied 10 pts (4M, 6F) aged 27.3 ± 10.9 yrs (range 16-44) who had undergone APF at 9.9 ± 7.6 yrs. All had sustained or recurrent arrhythmia for 5.0 ± 4.0 yrs. Scar was 19.9 ± 9.9% of recorded contact points, and atrial volume 202 ± 105 mls. EP studies were performed using simultaneous electroanatomic and non-contact mapping during sinus rhythm, atrial pacing at up to 6 sites, and atrial arrhythmia to identify fixed and functional conduction block, defined as a delay in wave front progression of >50ms, the presence of widely split potentials (>50ms) or cessation of wave front progression. Scar was defined as contact electrogram voltage <0.05mV. Fixed conduction block was present during all rhythms, whereas functional block was dependent on atrial cycle length and activation sequence. Results are expressed as mean ± SD.
Results: Twenty two arrhythmias were identified of cycle length (CL) 358 ± 117ms, which were macro-reentry (18), focal (3) and left atrial (1). Of the macro-reentrant circuits, 5 (26%) had evidence of functional block critical to arrhythmia maintenance, all at the putative position of the crista terminalis (CT), whereas 13 were dependent on fixed block - anterior wall scar (5), lateral wall scar (3), right AV valve patch (3), CT (2). No focal arrhythmia was successfully entrained. CL of circuits with functional block (267 ± 43ms) was significantly shorter than those without (384 ± 119ms) (p 0.005). Eight lines of functional block not maintaining circuits were seen at cristal (1) and non-cristal (7) sites. Functional circuits were associated with a smaller scar area (p 0.025), but not with age, age at APF or arrhythmia duration.
Conclusion: The crista terminalis is fundamental to the maintenance of certain macro-reentrant arrhythmias post APF. Specific ablative strategies which target this area may improve outcome in the long-term.

4:15 p.m.

830-4 **Focal Patterns of Activation in Patients with Atrial Tachycardias and Surgically Corrected Congenital Heart Disease.**

Natasja M. de Groot, Nico Blom, Wing King Chan, Ernst E. van der Wall, Martin Schalij, Leiden University Medical Center, Leiden, The Netherlands

Atrial tachycardias (AT) in pts with surgically corrected congenital heart disease (CHD) are often atrial flutter (AFL) or intra-atrial reentrant tachycardias (IART) with complex reentrant circuits embedded within areas of scar tissue. This study was aimed at characterising the underlying mechanisms of AT's in pts with surgically corrected CHD.
Methods: Mapping studies were performed in pts (n= 20, 28±9 yrs) with CHD and drug-refractory AT referred for catheter ablation. Extensive 3-D electro-anatomical mapping was performed during AT prior to ablation to 1) identify the underlying mechanism of the AT and 2) select target sites for ablation. Activation maps of the right atrium demonstrating a single (counter)-clockwise, cavo-tricuspid isthmus dependent macro-reentry circuit were labelled as typical atrial flutter (AFL). All other atrial macro-reentrant tachycardias were classified as scar-related AT (s-ART). Activation maps characterized by a radially spreading wavefront arising from one single site were defined as a focal atrial tachycardia (FAT). Successful ablation was defined as termination during ablation (IART and FAT) or the assessment of a bi-directional conduction block (AFL).
Results: Underlying CHD is transposition of the great arteries (n=9), tricuspid atresia (n=8) or both (n=3). Mapping revealed 35 different AT's including not only AFL (n=6, CL 257±36 ms) and s-ART (n=24, CL 289±74 ms) but also focal atrial tachycardia (FAT, n=5, CL 394±100 ms). FAT originated from the isthmus (n=1), superior part of the septum, high (n=2) and lower part of the antero-lateral wall (n=2). Fragmented electrograms were recorded at the site of origin of all FAT. Ablation of IART was successful in 66% of the pts and in all pts with AFL and FAT.
Conclusion: Underlying mechanism of AT in pts with surgically corrected CHD included not only macro-reentry giving rise to s-ART or AFL, but also focal activity. These focal patterns of activation can be the result of micro-reentry, triggered activity or enhanced automaticity.

4:30 p.m.

830-5 Spontaneous Termination Occurs In The Low Voltage Zone Produced By Pilsicainide -Analysis Of A Safety Factor Of Atrial Flutter

Kikuya Uno, Toru Iwa, Isao Kato, Yasushi Suzuki, Motoyuki Fukuta, Yasushi Wakita, Takayuki Ito, Kazuaki Shimamoto, Sapporo Medical University, Sapporo, Japan, Aichi Medical College, Aichi, Japan

Background: Few analyses of the effects of antiarrhythmic agents on atrial flutter have been reported using noncontact mapping to analyze low voltage zones (LVZ), conduction velocity (CV) and block lines. The aim of the study was to explore the role and relationship of the dynamic LVZ, CV and BL in the spontaneous termination of atrial flutter by the pure sodium channel blocker, pilsicainide by analysis with noncontact dynamic isopotential mapping (DIP-map).
Methods: A right atrial (RA) incision was produced and placed on RA free wall in nine canines weighing 25-37 kg. Bipolar pacing needle-pairs were placed on three sites of RA. A 9F noncontact multielectrode array catheter was deployed in RA via the femoral vein. Raw data were recorded during sinus rhythm, rapid atrial pacing and induced atrial flutter, and were superimposed onto the virtual 3-dimension-RA endocardium. Threshold of LVZ was set at 30% of the major peak negative (MPN) amplitude of RA. We analyzed LVZ, CV and block lines in DIP-map from the virtual electrograms. After inducing sustained stable atrial flutter, pilsicainide was administered intravenously (5-30mg, 5mg/5min). Then, spontaneous termination was obtained during data sampling. Relationship between LVZ, CV and block lines was also analyzed with the atrial MPN from the DIP-map and virtual electrograms.
Results: 1) Twenty-one episodes of atrial flutter were induced in 9 canines. 2) The cycle length of atrial flutter significantly prolonged from 163+/-19 to 214+/-12 ms ($p<0.05$). 3) The CV in the LVZ significantly changed before and after the PLS (1.6+/-0.6, 2.4+/-0.6 m/s, $p<0.05$). 4) The extent of the LVZ dynamically enlarged from 13.4+/-1.6 to 25.4+/-2.3 cm^2 ($p<0.05$) after pilsicainide. 5) The LVZ enlarged with the BL and was functionally prolonged by the PLS. 6) Spontaneous termination occurred in the LVZ with a prolonged CV. 7) Dynamic MPN progressed into the LVZ and conducted decrementally, and 8) termination was observed in the area of LVZ.
Conclusion: 1) PLS dynamically increased the extent of the LVZ, increasing the length of the block line and the delay of CV. 2) The decremental conduction in LVZ can be the crucial factor for atrial flutter termination.

4:45 p.m.

830-6 Results from Electrophysiological and Pharmacological Assessments Suggest Concealed Atrio-Hisian Fibers Constitute Retrograde Limbs in Reentrant Circuits of Slow-Fast Type Atrioventricular Nodal Reentrant Tachycardias in One-third of Patients

Kiyoshi Otomo, Kazuhiro Suyama, Takashi Noda, Eiichiro Nakagawa, Kazuhiro Satomi, Wataru Shimizu, Takashi Kurita, Naohiko Aihara, Shiro Kamakura, National Cardiovascular Center, Suita City, Japan, Tokyo Medical and Dental University, Tokyo, Japan

Backgrounds: Some of the retrograde fast pathways (rFPs) in slow-fast type AV nodal reentrant tachycardias (AVNRTs) have been reported to exhibit little decremental property with short VA conduction time and high 2:1 VA block (VAB) rate and to be resistant to agents that suppress AV nodal conduction. The mechanisms for these "Kent bundle-like behaviors"of rFPs, however, have not been clearly elucidated.
Purposes: To characterize rFPs both electrophysiologically and pharmacologically and to elucidate the mechanisms by which rFPs behave like Kent bundles.
Methods & Results: Seventy-four patients with AVNRT were classified into 2 groups according to the responses of rFP conductions to boluses of 20mg of adenosine triphosphate (ATP) into inferior vena cava during RV pacing (100-120ppm); ATP-S (47 patients, 63.5%): VAB and ATP-R (27 patients, 36.5%): no VAB. During incremental pacing from RV, all patients in ATP-R showed fixed HA intervals at all paced cycle lengths upto development of 2:1 VAB, while ATP-S patients showed a little decremental property with prolongation in HA intervals at shorter paced cycle length (increments of HA intervals; ATP-R: 2±2ms vs ATP-S: 35±33ms, $p<0.05$). HA intervals were also measured during AVNRT (HAt) and entrainment from paraHisian RV without direct His bundle capture (HAe). It has been postulated that HAt would be the difference in conduction times between rFP (y) and lower common pathway (x) (HAt=y-x), whereas HAe would be the sum of them (HAe=y+x). Hence, x=(HAe-HAt)/2. x of >0 would suggest presence of lower common pathway between lower turnaround and His bundle, whereas x of <0 would suggest absense of lower common pathway and the participation of concealed atrio-Hisian fiber as retrograde limb of reentrant circuit. As a result, x was significantly less in ATP-R than in ATP-S (-6±5 vs 4±4ms, $p<0.05$) and was <0 in 23 patients (85%) of ATP-R. Among 25 patients with x<0, 23 patients (92%) were classified into ATP-R.
Conclusions In one-third of AVNRTs, rFPs were shown to originate from His bundles and exhibit non-decremental property with resistance to ATP, suggesting that these rFPs might consist of concealed atrio-Hisian fibers totally bypassing AV nodes.

5:00 p.m.

830-7 Evidence of Mechanoelectric Feedback in the Atria of Patients With Atrioventricular Nodal Reentrant Tachycardia

Emmanuel G. Manios, Emmanuel M. Kanoupakis, Hercules E. Mavrakis, Ioannis K. Karalis, Dimitris A. Arfanakis, Eleftherios Kallergis, Panos E. Vardas, Heraklion University Hospital, Heraklion, Greece

Background: AV nodal reentrant tachycardia (AVNRT) could serve as a clinical model to study the effects of mechanical stretch on the electrical properties of the human atrium.
Methods: We assessed 11 consecutive pts with AVNRT, admitted for RF ablation, atrial pressure (Pa) and atrial refractoriness (AERP) at right atrial appendage and lateral wall during atrial pacing at 3 basic cycle lengths (600, 500, 400 ms) and after 2 min of pacing at the cycle length of tachycardia. Measurements were repeated from the same position, after ventricular pacing and after 2 min of tachycardia.
Results: Peak, mean and minimal Pa increased from 6,2,0 mmHg at baseline to 9,5,2 mmHg during atrial pacing at the cycle length of tachycardia. During ventricular pacing the Pa were 16,10,1 mmHg respectively and remained substantially unchanged when AVNRT was induced. A significant reduction in AERP was observed during ventricular pacing compared with baseline values (table 1). Two mins of spontaneous AVNRT changed the AERP to values significantly lower than those during atrial pacing at the cycle length of tachycardia at both sites (from 216±13 to 194±16ms, and from 212±15 to 192±17ms, $p=0.004$ and $p=0.004$, at the appendage and the lateral wall respectively).
Conclusions: AVNRT and ventricular pacing significantly increase Pa and subsequently shorten AERP and increase its dispersion. These findings provide evidence that mechanoelectrical feedback plays an important role in the occurrence of reentrant atrial arrhythmias.

Table 1

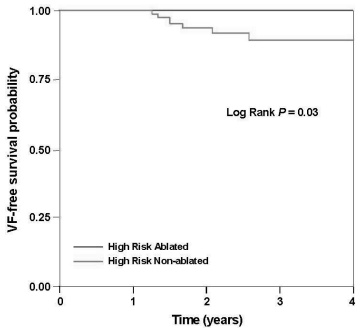
	RA appendage			RA lateral wall		
	600 ms	500 ms	400 ms	600 ms	500 ms	400 ms
Baseline	228±22	224±23	218±24	217±21	211±24	209±23
V pacing	212±31	207±28	192±26	208±25	198±21	190±24
p	0.046	0.01	0.039	0.042	0.045	0.043

5:15 p.m.

830-8 Prophylactic Catheter Ablation Reduces the Risk of Ventricular Fibrillation As First Clinical Presentation In The Asymptomatic WPW Syndrome

Carlo Pappone, Francesco Manguso, Giuseppe Augello, Amedeo Ferro, Gabriele Paglino, Gabriele Vicedomini, Nicoleta Sora, Vincenzo Santinelli, San Raffaele University Hospital, Milan, Italy

Background - Ventricular fibrillation (VF) may be the first clinical arrhythmia among asymptomatic WPW subjects.
Methods - We pooled data from our 3 recent studies in *JACC* and *NEJM*. In all studies, patients underwent an electrophysiologic testing for risk stratification. In the *JACC* study 47 high-risk subjects were identified; in the 2 *NEJM* trials, 119 high risk subjects were randomized to catheter ablation or no treatment.
Results -Ventricular fibrillation occurred in 7 subjects (4%), all among *high risk non-ablated* subjects (*Figure*). The characteristics of these subjects are reported in *Table*.
Conclusions - Asymptomatic WPW is not too benign, as previously thought. Prophylactic ablation among high-risk asymptomatic patients should be considered mandatory to prevent sudden death.



Patients with VF

Variable	Patient #1	Patient #2	Patient #3	Patient #4	Patient #5	Patient #6	Patient #7
Age (yr)	25	21	22	22	10	8	12
Male sex	M	F	M	M	M	M	M
Structural heart disease	no	no	no	no	no	no	no
APERP (ms)	250	230	220	220	210	220	210
Multiple AP	yes	yes	yes	yes	yes	yes	yes
Inducibility	yes	yes	yes	yes	yes	yes	yes
AVRT triggering AF	yes	yes	yes	yes	yes	yes	yes
AVRT cycle (ms)	250	260	250	240	220	230	220
SPRR during sustained AF (ms)	230	230	220	200	200	190	200

ORAL CONTRIBUTIONS

838FO Featured Oral Session... Ablation of Atrial Fibrillation: Avoiding Esophageal Injury

Tuesday, March 08, 2005, 8:30 a.m.-10:00 a.m.
Orange County Convention Center, Room 232A

8:45 a.m.

838-4 Assessment Of The Highly Variable Course Of The Esophagus And Its Proximity To The Left Atrial Endocardium by 3D CT Scan

Jennifer E. Cummings, Nassir F. Marrouche, Robert Schweikert, Walid Saliba, Atul Verma, Fethi Kilicaslan, J. David Burkhardt, William A. Belden, David O. Martin, Oussama Wazni, Dhanumjaya Lakkireddy, Andrea Natale, The Cleveland Clinic Foundation, Cleveland, OH

Background: Left atrial-esophageal fistula remains one of the most devastating and fatal complications of atrial fibrillation ablation. There is no standard approach to identifying esophagus (Eso) location prior to ablation.
Objective: To evaluate and compare different modalities for determining anatomical variation and proximity of Eso to the posterior wall of the left atrium (LA)
Methods: Cardiac CT images in fifty patients presenting for pulmonary vein antrum isolation (PVAI) were reviewed. The closest distance between the LA endocardial surface and Eso lumen was measured in each patient. The location of this closest approximation was categorized in location as right-inferior, right-superior, mid-inferior (between the right and left inferior antrums), left-inferior, and left superior. In 7 patients an esophageal electrode was placed at initiation of the procedure and a 3-D mapping and navigation (NAVX) was used to identify the course of the Eso during electrode pullback.
Results: Thirty-eight of the 50 patients were male. Mean ejection fraction was 0.52±0.8 and age was 48.3±24 years. The area of closest LA-Eso contact was dermined to be in the right inferior PV antrum in 10(20%), right superior in 1(2%), mid-inferior in 19(38%), left superior in 5(10%), and left inferior in 15 (30%) patients. The mean distance at closest approximation between LA endocardium and the ESO lumen was 4.4mm±1.2mm. Three patients had a LA-Eso distance of 2.8mm. In patients where NAVX was used, the Eso course was consistent with that documented on the 3-D CT scan in all patients.
Conclusions: There is a significant variability in the location of closest LA-Eso contact. These locations can be close to the PV antral regions. The area of closest contact between the LA and Eso may be <3mm. 3D NAVX mapping can be readily used to document the course of the Eso in relationship to the LA. Integration of 3D-CT scans into maping systems may be a reliable tool in identifying areas of increased risk for LA-Eso perforation during RF applications.

9:00 a.m.

838-5 Avoiding Esophageal Injury With Power Titrating During Left Atrial Ablation for Atrial Fibrillation: An Intracardiac Echocardiographic Imaging Study

Jian-Fang Ren, David J. Callans, Francis E. Marchlinski, Hemal Nayak, David Lin, Edward P. Gerstenfeld, University of Pennsylvania, Philadelphia, PA

Injury to esophagus (Eso) has occurred during left atrial (LA) ablation for atrial fibrillation (AF) since the LA posterior wall (PW) is immediately contiguous to Eso wall (LAPW-Eso). The aim of this study is to evaluate lesion morphologic and wall thickness changes with radiofrequency (RF) delivered at LAPW-Eso wall using AcuNav intracardiac echocardiography (ICE). Methods and Results: ICE was performed in 42 patients (age 56±12 years, 33 men) with AF undergoing RF LA pulmonary vein (PV) electric isolation using 8mm electrode (70W, up to 50-52°C, 60sec) or Chili catheter (up to 40°C, 60sec). With ICE transducer placed in the right atrium and scanning between the lower right and left PV ostia, a longitudinal imaging view of the LAPW-Eso region was obtained in all patients. There was 4.3±3.2 lesions/patient delivered to this region during RF at PW around the lower/middle right and lower left PV ostia. The RF lesion morphologic changes were observed with wall swelling, dimpling, crater or echogenic enhancement. The LAPW-Eso wall thickness and changes in echogenic lesion thickness were measured Pre- and Post-RF lesions under routine circumstance (n=44) and during RF power titration (PT, n=29) using ICE monitoring (Table). Conclusions: RF lesions with 8mm electrode or chili catheter delivered at LAPW-Eso wall induced echogenic lesion morphologic changes involving Eso anterior wall. Echogenic lesion morphologic changes may be controlled and limited within LAPW with power titrating under ICE lesion monitoring.

	LAPW-Eso Wall	Echogenic wall thickness Post-RF	Echogenic wall thickness Post-RF PT
Mean±SD(mm)	6.1±0.9	10.8±2.2	4.8±1.5*
Range (mm)	5.0-8.5	7.0-15.0	3.0-8.3
*p<0.01:vs. Post-RF			

9:15 a.m.

838-6 Computerized Tomographic Analysis of the Anatomy of the Left Atrium and the Esophagus: Implications for Left Atrial Catheter Ablation

Kristina Lemola, Michael Schneider, Benoit Desjardins, Ian Case, Jihn Han, Eric Good, Kamala Tamirisa, Ariane Tsemo, Aman Chugh, Frank Bogun, Frank Pelosi, Jr., Ella Kazerooni, Fred Morady, Hakan Oral, University of Michigan, Ann Arbor, MI

Background: During left atrial catheter ablation, an atrio-esophageal fistula can develop due to thermal injury of the esophagus during ablation along the posterior left atrium (LA). No *in vivo* studies have examined the relationship of the esophagus to the LA. The purpose of this study was to describe the topographical anatomy of the esophagus and the posterior LA using computerized tomography (CT).
Methods: A spiral CT of the chest with 3-D reconstruction was performed in 50 patients (mean age = 54 ± 11 years) with atrial fibrillation (AF) prior to an ablation procedure. Consecutive axial and sagital sections of the CT scan were examined to determine the relationship, size and thickness of the tissue layers between the LA and the esophagus.
Results: The mean length and width of the esophagus in contact with the posterior LA were 58 ± 14 mm, and 13 ± 6 mm, respectively. The esophagus had a variable course along the posterior LA. The esophagus was close (10 ± 6 mm from the ostia) and parallel to the left-sided pulmonary veins (PVs) in 56% of patients and had an oblique course from the left superior PV to the right inferior PV in 36% of patients. The mean thickness of the posterior LA and anterior esophageal walls were 2.2 ± 0.9 mm, and 3.6 ± 1.7 mm, respectively. In 98% of patients, there was a fat layer between the esophagus and the posterior LA. However, this layer often was discontinuous.
Conclusions: The esophagus and posterior LA wall are in close contact over a large area that may often lie within the AF ablation zone, and there is marked variation in the anatomical relationship of the esophagus and the posterior LA. Both the esophageal and atrial walls are quite thin. However, a layer of adipose tissue may serve to insulate the esophagus from thermal injury, explaining why atrio-esophageal fistulas are rare.

9:30 a.m.

838-7 Esophageal Imaging Characteristics and Structural Measurement During Left Atrial Ablation for Atrial Fibrillation: An Intracardiac Echocardiographic Study

Jian-Fang Ren, Francis E. Marchlinski, David J. Callans, University of Pennsylvania, Philadelphia, PA

The esophagus (Eso) is immediately contiguous to the left atrial (LA) posterior wall (PW). Eso injury has been noted with inadvertent LA ablation for atrial fibrillation (AF). The aim of this study is to confirm Eso imaging features and quantify the Eso region contiguous to the LAPW (Eso-LAPW) using AcuNav intracardiac echocardiography (ICE). Methods and Results: We studied Eso imaging and measured Eso-LAPW structures using ICE in 42 patients (age 56±12 years, 33 men) with AF undergoing LA ablation. With ICE transducer placed in the right atrium and scanning between the lower right and left pulmonary vein ostia, a longitudinal imaging view of the Eso-LAPW region was obtained in all patients. A variety of Eso imaging features including gas, fluid-filled, movement within its segments, or collapsed lumen was identified with real-time ICE imaging during ablation procedure. Eso fluid-filled, movement or saliva swallowing, all enhanced the Eso imaging. In all fasted patients, Eso gas caused significant scattering of the ultrasonic beam, thus temporarily/partially obscuring its deeper structure- the Eso PW in 25% patients. The Eso-LAPW length, Eso diameter and anterior wall, LAPW and LA diameter were measured with ICE imaging (Table). The Eso-LAPW length correlated to the LA diameter (r=0.78, p<0.01). Conclusions: Eso and Eso-LAPW region can be easily identified with ICE imaging. Real-time ICE imaging of Eso-LAPW region may provide an important monitoring for avoiding inadvertent Eso injury during LA ablation.

(mm)	Eso-LAPW length	Eso diameter	Eso wall	LAPW	LA diameter
Mean±SD(mm)	26.5±6.5	16.6±3.2	3.4±0.5	2.7±0.5	48±5
Range (mm)	15.0-47.0	9.0-22.0	2.5-4.5	2.0-4.0	38-63

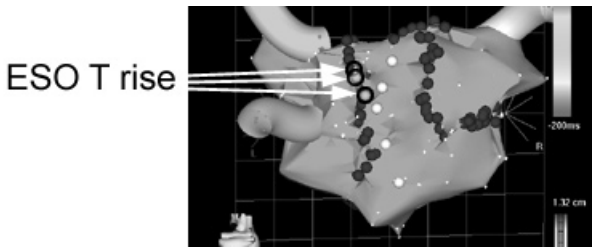
9:45 a.m.

838-8 Esophageal Temperature Monitoring During Left Atrial Catheter Ablation for Atrial Fibrillation

David Cesario, Kalyanam Shivkumar, Miguel Valderrabano, Isaac Wiener, Charles Swerdlow, UCLA Medical Center, Los Angeles, CA, Cedars Sinai Medical Center, Los Angeles, CA

Background: Left atrial (LA) - esophageal (ESO) fistula is a life-threatening complication of LA radiofrequency catheter ablation (CA) for atrial fibrillation. We hypothesized that monitoring of ESO temperature (T) may detect early T rises to prevent ESO injury.
Methods: We inserted an ESO T probe during LACA in 12 pts. The course of the ESO was marked on electroanatomic maps at the closest points on biplane fluoroscopy. The T probe was positioned at the level of the 8-mm ablation tip for lesions on the posterior wall or roof, where maximum power and T were 40 - 50 W/50 - 55°. We stopped ablation for an abrupt rise in ESO T >0.5°. **Results:** Abrupt ESO T rises occurred in 11 pts (92%) at 1 - 4 locations after 15 - 60 sec of ablation. ESO T rose for ~ 30 sec after termination of ablation by a maximum of 1.3 ± 0.3° (range 0.8 - 1.6°). Ablation sites with ESO T rises corresponded to the course of the ESO on electroanatomic maps, but were part of 3 different sets of linear lesions: LA-roof ablation line (2 pts) or encircling lines around left-sided (7 pts) or right-sided (2 pts) pulmonary veins. The Figure shows a typical electroanatomic map (posterior-anterior projection) with ablation sites (black), ESO (white), and sites of T rise (arrows). There were no acute or chronic complications. **Conclusions:** ESO T rises abruptly during LACA at sites adjacent to the ESO. T rises were associated with 3 different

lesion sets. The maximum T rise was small when ablation was stopped for a T increase of 0.5°. Monitoring ESO T may reduce the risk of LA-ESO fistula.



POSTER SESSION

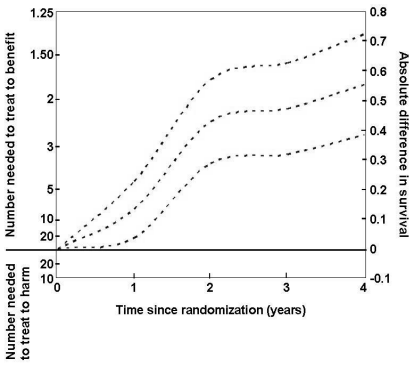
1135 Ablation of Supraventricular and Atrial Tachycardias

Tuesday, March 08, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 11:00 a.m.-Noon

1135-257 Pooling Data Analysis To Identify The Number Needed To Treat For Prevention Of Arrhythmic Events In High-risk Asymptomatic WPW

Carlo Pappone, Francesco Manguso, Giuseppe Augello, Amedeo Ferro, Valter Tortoriello, Gabriele Vicedomini, Vincenzo Santinelli, San Raffaele University Hospital, Milan, Italy

Background - Individual studies on asymptomatic WPW may be limited by small sample sizes for end points with relatively low incidences.
Objectives - To synthesize all available data by pooling data from our two recent randomized studies published in the *New England Journal of Medicine*.
Methods - In both studies, all patients underwent an electrophysiologic testing (EPT) for risk stratification. Inducible subjects were considered at high-risk and thereafter randomized to catheter ablation or no treatment. By pooling all data, there were 119 high-risk and 253 low-risk patients.
Results - Overall, 69 of 315 (22%) untreated subjects developed during follow-up arrhythmic events. By Kaplan-Meier analysis, arrhythmic events occurred in more than 60% of high-risk untreated subjects as compared to the 5% of ablated patients ($p<0.001$).
The number of high-risk patients needed to treat, calculated according to the method by Altman et al., to prevent arrhythmic events in one high-risk patient was 7.6 at one year, 2.3 at 2 years and 1.8 at 4 years (Figure).
Conclusions - Therefore, performing ablation in high-risk asymptomatic patients would lead to one event-free patient at 2 years for every 2.3 patients ablated. These results are clinically important as they demonstrate that ablation among high-risk asymptomatic patients is of durable benefit and not harm at any point during follow-up.



1135-258 Remote-controlled Catheter Ablation Of Common Type AVNRT Using The New Niobe Magnetic Navigation System

Sabine Ernst, Julian Chun, Feifan Ouyang, Matthias Antz, Karl-Heinz Kuck, St. Georg Hospital, Hamburg, Germany

Introduction: Atrio-ventricular nodal re-entrant tachycardia (AVNRT) can be cured by a focal radiofrequency current (RFC) applications. The new Niobe magnetic navigation system consists of two computer-controlled permanent magnets located on opposite sides of the patient table, and an ablation catheter equipped with one or three magnets which align with the user-defined magnetic field direction (0.08 Tesla). A motor drive, controlled via joystick, advances or retracts the catheter, thus enabling complete remote navigation.
Methods: A total of 71 pts (23 m, mean age 50 ± 16 years) were enrolled in the initial study using either the single (1M, 55 pts) or a three magnet (3M, 16 pts) ablation catheter and had documented episodes of common-type atrial flutter. Both ablation catheters consist of a 4 mm solid tip to perform radiofrequency current (RFC) ablation (55°C, max 40 W, 60 - 120 sec).
Results: In all pts, remote-controlled mapping of the target area successfully and safely performed. Using the 1M catheter, slow pathway modulation or ablation was achieved in all pts with mean procedure duration of 150 ± 48 min (mean RFC 7 ± 4.6, mean fluoroscopy time 10.3 ± 8.5 min). Using the second generation 3M catheter with improved deflection properties, further shortening of procedure duration (123 ± 39 min) and necessary fluoroscopy (6.4 ± 2.5 min) could be demonstrated, while using 6.5 ± 3.7 RFC applications. There were no associated complications.
Conclusions: The Niobe system is a new platform technology allowing the remote-controlled navigation using a 4 mm tip ablation catheter for both slow pathway modulation and ablation was safely and effectively performed in pts with typical atrio-ventricular nodal re-entrant tachycardia. By addition of two more magnets to the tip, catheter deflection force improved the catheter tissue contact, which resulted in improved procedural parameters such as fluoroscopy time, number of RFC applications and procedure duration.

1135-259 Cryoablation of Supraventricular Tachycardia in Children and Adolescents: Predictive Value of Cryomapping

Thomas A. Kriebel, Claudia Broistedt, Maja Kroll, Christian Jux, Thomas Paul, Georg-August-University, Göttingen, Germany

Background: Recently, cryoenergy application has evolved as a safe and effective alternative for ablation of arrhythmia substrates. Two specific features of this technique make it very attractive for pediatric patients: prediction of the effect of energy application by creating reversible block of conduction (cryomapping) and avoidance of dislodgment of the catheter by freezing of the catheter tip to the endocardium (cryoadhesion) therefore minimizing the risk of complications and the time of fluoroscopy. The aim of the study was to analyse the predictive value of cryomapping in pediatric patients.
Methods: Since July 2003 31 patients (mean age 10.1 years) underwent electrophysiological study for symptomatic supraventricular tachycardia under the guidance of the Loca Lisa® system. After identification of the arrhythmia substrate (AVNRT=12; accessory pathways (AP)=19) cryomapping was performed using the Freezor® 4 mm or Freezor Xtra® 6 mm tip catheter with a target temperature of -30 ºC for a maximum of 60 seconds. If cryomapping was successful, cryoenergy was delivered at the same spot at -75 ºC verified by the Loca Lisa® system for a total of four minutes (cryoablation).
Results: In 23 of the 31 patients (74.21%) cryoablation was successful (AVNRT: 10/12, AP 13/19). A median of 2 (1-10) cryoablations were delivered. In the 8 remaining patients, radiofrequency catheter ablation was effective in 5 (overall success rate 90.3%). In 4 patients with an AP cryomapping was unsuccessful. However, cryoablation resulted in AP interruption within 30 seconds at the identical location verified by the Loca Lisa® system. In addition, in 3 patients with AVNRT transient high grade AV-block occurred during cryoablation despite previous “safe” cryomapping at the same location.
Conclusion: According to our results cryomapping was not effective to predict cryoablation outcome in 7 out of 31 patients studied. These results may in part be explained by a smaller and therefore insufficient lesion size during cryomapping.

1135-260 Prognostic Implication of Progressive Isthmus Conduction Delay During Successful Radiofrequency Current Application for Atrial Flutter

Yuji Okuyama, Takafumi Oka, Taku Sakai, Atsushi Hirayama, Kazuhisa Kodama, Osaka Police Hospital, Osaka, Japan

Aims: Cavotricuspid isthmus conduction (CIC) can be blocked completely with an abrupt prolongation of conduction time or with a gradual increase in conduction time during successful radiofrequency current (RFC) application for common atrial flutter (AFL). This study sought to assess the prevalence and characteristics of a gradual increase in conduction time during successful RFC application and to define its predictors and its relationship with the results of long-term follow-up.
Methods and results: A total of 104 consecutive patients (76 men, 28 women, mean age 60 ± 13 years) who underwent successful AFL ablation were included. The procedure endpoint was defined as complete bi-directional CIC block. Successful CIC block was achieved in 156 RFC applications in which CIC recurrence was observed after 52 RFC applications. During successful RFC applications, the incidence of a gradual increase in conduction time, defined as more than 20% increase in time from pacing stimuli from coronary sinus ostium to the atrial potential just lateral to the presumed blocking line before complete CIC block during successful application of RFC, was 7.7% (8/104) in patients and 13.5% (21/156) in applications with CIC block. CIC block with a gradual increase in conduction time had a higher incidence of acute CIC resumption than those with an abrupt prolongation of conduction time (16/21 vs 36/135, $p<0.05$). The AFL recurrence rate was 5.8% (6/104) during a mean follow-up period of 13 ± 5 months. Patient with a gradual increase in conduction time had a higher incidence of AFL recurrence than those with an abrupt prolongation of conduction time (3/8 vs 3/96, $p<0.01$)
Conclusions: Our results suggest that a gradual increase in conduction time may be a potential risk for acute CIC resumption and clinical AFL recurrence during long-term follow-up. Observation time should be prolonged if a gradual increase in conduction time was observed during the application with CIC block.

1135-261 **Post-Operative Atrial Tachycardias in Patients with Mitral Valve Disease: what is the Location of the Arrhythmogenic Substrate ?**

Natasja M. de Groot, Nico Blom, Ernst E. van der Wall, Martin Schalij, Leiden University Medical Center, Leiden, The Netherlands

Introduction: Atrial tachycardias (AT) in patients who underwent cardiac surgery for mitral valve disease (MVD) commonly originate from the left atrium. In this study, we analysed the underlying mechanism of the AT and the location of the arrhythmogenic substrate in patients with MVD and post-operative AT.
Methods: Electro-anatomical mapping of post-operative, drug-refractory AT's was performed in pts (n=15, 8 male, age 55±12[43-74] yrs.) who had undergone cardiac surgery for MVD prior to ablation. Mapping was aimed at elucidating the underlying mechanism of the AT and to select target sites for ablation. Peak-to-peak voltages of bipolar electrograms were off-line analysed. Activation maps of the right atrium demonstrating a single (counter)-clockwise, cavo-tricuspid isthmus dependent macro-reentry circuit were labelled as typical atrial flutter (AFL). All other atrial macro-reentrant tachycardias were classified as scar related-AT (s-AT). Activation maps characterized by a radially spreading wavefront arising from one single region were defined as a focal atrial tachycardia (FAT).
Results: Seventeen different AT's were mapped and ablated. All AT's originated from the right atrium. Activation maps revealed a FAT (CL 280±66 ms, n=4/(24%)), s-AT (n=3/17%, CL 271±45 ms) or (AFL n=10/(59%), CL 235±60 ms). FAT were successfully ablated at the site of earliest endocardial activity. A bi-directional conduction block was assessed in all pts with AFL. s-AT was successfully ablated in 2/3 (66%) of the pts.
Conclusion: AT observed in MVD patients include not only s-AT but also AFL and FAT. Surprisingly, the arrhythmogenic substrate was located in the right atrium in all patients.

1135-262 **Response to Adenosine Differentiates Atrial and Ventricular Tachycardias by Mechanism**

Bindi K. Shah, Sei Iwai, Steven M. Markowitz, Suneet Mittal, Kenneth M. Stein, Ravi K. Yarlagadda, Jim Cheung, Vivian Tan, Bruce B. Lerman, Cornell University Medical Center, New York, NY

Background: Differentiation between reentrant and nonreentrant tachycardias and the relative dimensions of the tachycardia circuit (macro vs. focal) are demonstrated by entrainment (a relatively insensitive test) and multisite mapping.
Objectives: We hypothesized that adenosine (ADO) is a sensitive and specific mechanistic probe in atrial and ventricular tachycardia (AT and VT), differentiating between focal nonreentrant and macroreentrant circuits.
Methods: To this end, we examined the effects of ADO on 152 sustained tachycardias in 150 patients (54±14 years of age; 86 males): 74 ATs and 78 VTs. The mechanism of tachycardia was characterized by entrainment, 3D electroanatomic mapping, and results of successful radiofrequency ablation, as well as response to verapamil. The initial dose of ADO was determined by weight and titrated for definitive effect on the conduction system.
Results: The overall sensitivity and specificity of using ADO to determine whether an arrhythmia has a focal (nonreentrant) origin are 94% and 100%, respectively. For AT, the sensitivity and specificity are 98% and 100%, respectively. For VT, the sensitivity and specificity are 89% and 100%, respectively.

Response to Adenosine

	AT Focal	AT Nonfocal	VT Focal	VT Nonfocal
ADO Sensitive	53	0	47	0
ADO Insensitive	1	20	6	25

Conclusions: ADO has mechanism-specific effects on both AT and VT. Sensitivity of AT or VT to ADO is consistent with a nonreentrant mechanism and focal origin.

POSTER SESSION

1136 Cardiac Resynchronization Therapy: Outcomes

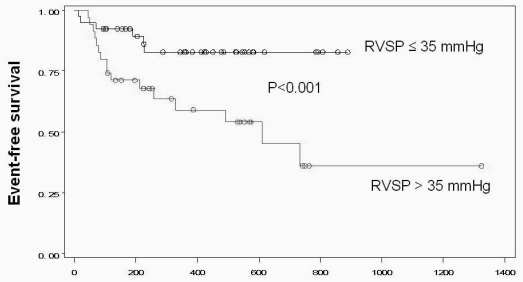
Tuesday, March 08, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 11:00 a.m.-Noon

1136-267 **Echocardiographic Peak Right Ventricular Systolic Pressures Predict Adverse Outcomes in Cardiac Resynchronization Therapy**

Usha B. Tedrow, Daniel Kramer, Lynne W. Stevenson, William G. Stevenson, Kenneth L. Baughman, Laurence M. Epstein, Eldrin F. Lewis, Brigham and Women's Hospital, Boston, MA

Background: Cardiac resynchronization therapy (CRT) can improve outcomes in 2/3 Class III or IV heart failure pts. We hypothesize poorer survival in patients (pts) with elevated right heart pressures.
Methods: We evaluated echo, ECG and clinical records from 75 consecutive CRT pts. RV systolic pressure (RVSP) was calculated from peak tricuspid regurgitant time velocity profile. The primary endpoint was a composite of mortality, cardiac transplant, or LV assist device (22 events). Kaplan-Meier curves, log-rank test and Cox proportional hazard ratios (HR) were used to evaluate events and pt characteristics.
Results: Pts were grouped by RVSP > or ≤ 35 mmHg. Clinical features were similar between groups, except for more chronic renal insufficiency (CRI) and RV dysfunction when RVSP >35 mmHg.
Univariate analysis identified diabetes (HR 2.45), CRI (HR 3.52), AF (HR 3.07), use of non-amiodarone anti-arrhythmics (HR 2.86), atrial pacing (HR 2.57), and prolonged PR interval (HR 1.009) as associated with poorer survival. Sinus rhythm (HR 0.34), LBBB (HR 0.44), and beta-blocker use (HR 0.47) were associated with improved survival. Three variables remained significant in a multivariable model - high RVSP, (HR 3.71 95% CI 1.31, 10.4), CRI (HR 3.18, 95% CI 1.29, 7.86) and AF (HR 4.22, 95% CI 1.54, 11.6).
Conclusions: RVSP >35 mmHg is associated with > 3-fold risk of decreased survival, which may reflect elevated left-sided pressures, pulmonary hypertension, or RV failure. High RVSP may guide choice of therapy in CRT candidates.

Figure: Time to Death, Transplant or LVAD in CRT pts with high and low RVSP



1136-268 **Cardiac Resynchronization Therapy Improves Pulmonary Hypertension in Congestive Heart Failure**

Yong-Mei Cha, Robert F. Rea, Win-Kuang Shen, Samuel J. Asirvatham, David M. Turnbull, Linda K. Hyberger, David L. Hayes, Mayo Clinic, Rochester, MN

Background: Pulmonary hypertension (PHT) is frequently present in patients (pts) with advanced congestive heart failure (CHF). Although trials have demonstrated that cardiac resynchronization therapy (CRT) improves left ventricular (LV) function and symptoms of CHF, little is known the impact of CRT on PHT. The aim of this study was to determine the hemodynamic effect of CRT on pulmonary artery systolic pressure (PASP) along with LV systolic function in pts with CHF.
Methods: Database of 254 pts who received CRT at the Mayo Clinic during 1/2002 to 12/2003 was screened. Sixty-three pts (male 51, female 12, mean age 65±11 yrs) had pre-implant evaluation and post-implant follow-up at our institution. Transthoracic echocardiograms were performed to assess PASP, LVEF, and LV diastolic dimension. PASP was determined by right ventricle-right atrium gradient that was calculated by using the simplified Bernoulli equation. NYHA function class was assessed.
Results: The PASP was significantly reduced by CRT, along with improvement in LVEF and NYHA function class (see table). Twenty-nine of 63 pts (46%) had moderate to severe PHT ranging 51 to 84 mmHg prior to CRT. The PASP in these pts was significantly decreased from 62±10 to 49±16 mmHg (p=0.00003).
Conclusion: CRT reduces PASP in pts with advanced CHF, accompanied with improvement of LV systolic function and reversal of LV remodeling. The favorable response of PHT to CRT may provide an important insight to the symptomatic and functional improvement of CHF.

	Pre-CRT	Post-CRT	P
Pulmonary artery systolic pressure mmHg	51±15	44±14	0.002
LV ejection fraction %	21±7	27±10	<0.0001
LV diastolic dimension mm	69±10	65±9	0.002
NYHA class	3.0±0.6	2.3±0.9	<0.0001

1136-269 **Lead Proximity to Infarct Site Does Not Affect the Hemodynamic Response to Cardiac Resynchronization Therapy**

Daniel Arzola-Castaner, Cynthia Taub, E. Kevin Heist, Dali Fan, Michael H. Picard, Jeremy N. Ruskin, Jagmeet P. Singh, Massachusetts General Hospital, Boston, MA

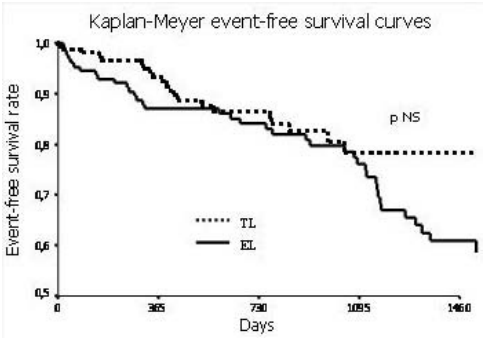
Background: Current reports suggest that the optimal pacing site for cardiac resynchronization therapy (CRT) is in the region of the left ventricular lateral wall. Although pacing in the infarct site could impact the contractile response to CRT, there is little information regarding the acute hemodynamic effects of CRT, when the left ventricular lead lies either distant from or on the infarct site.
Methods: 38 consecutive patients (8 female, age 70 ± 10 years, EF 22 ± 6%), with ischemic cardiomyopathy underwent biventricular pacemaker implantation for standard indications and were included in the analysis. Echocardiographic assessment of contractility was measured by Doppler profiles of mitral regurgitation as a percentage change in dP/dt (dP/dt) with CRT on and off. A standard echocardiographic protocol was used for myocardial segmentation and scoring of the wall motion abnormalities. Regions of akinesia and/or dyskinesia were identified as prior infarct sites. LV lead position in relation to the infarct site was determined by the consensus of three different cardiologists. LV leads were categorized as being on (group 1) or off the infarct site (group 2). Acute responders were defined as ΔdP/dt > 25%.

Results: The magnitude of the hemodynamic response to CRT was similar in group 1 (n=15) and group 2 (n=23). There was no significant difference in the baseline dP/dt (Group 1, 661.3±235.1 vs, Group 2, 659.9+ 210.4 p=0.99) or dP/dt (Group 1; 48.3 ± 71.1% vs. Group 2; 31.9 ± 40.1%, p = 0.46). Lead placement in posterolateral (PL) or lateral (LL) positions was associated with better hemodynamic response when compared to anterolateral (AL) positions irrespective of proximity to scar (dP/dt, PL, 50 ± 53% and LL, 29 ± 39 % vs. AL, -7 ± 23% respectively p < 0.05). LV lead on or off the infarct site did not distinguish between acute responders and nonresponders to CRT.
Conclusion: LV lead proximity to the infarct site is not a determinant of acute hemodynamic response to CRT. Optimal hemodynamic response may be obtained by LV lead placement in the lateral or posterolateral region irrespective of its proximity to the infarct.

1136-270 Long-Term Outcome in Heart Failure Patients Treated With Cardiac Resynchronisation Therapy: a Comparison Between Transvenous and Epicardial Leads

Santi Raffa, Cecilia Fantoni, Francois Regoli, Mihoko Kawabata, Helmut Klein, Angelo Auricchio, University Hospital, Magdeburg, Germany, University Hospital, Messina, Italy

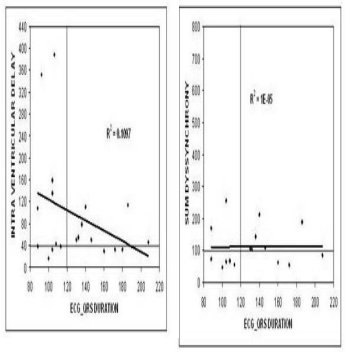
Background: Long term outcome of heart failure patients (pts) implanted with different left ventricular lead types [transvenous, (TL) vs epicardial, (EL)] is still unknown.
Methods: We compared improvement of functional capacity and echo parameters at 1 year follow-up and long term event free survival rate in 89 pts consecutively implanted with a TL and in 82 pts consecutively implanted with an EL. Events considered for the survival rate analysis were death for any cause, heart transplantation and left ventricular (LV) assist device implantation.
Results: Prevalence of male gender was higher among pts implanted with a TL (p<0,04). At baseline pts implanted with a TL had a lower LV ejection fraction (20±6 vs 22±7 %, p<0,01) and a higher pulmonary artery systolic pressure (43±17 vs 39±15 mmHg, p<0,05). There were no differences between the two groups in the other clinical, echocardiographic and hemodynamic variables. At one year follow-up pts with a TL showed a significant higher percentage increase of LV ejection fraction (46±61 vs 22±44 %, p<0,01) and of peak oxygen consumption (24±24 vs 11±28 %, p<0,03). Over a mean follow-up time of 762±581 days the event-free survival rate as assessed by Kaplan-Meyer curves was not significantly different between the two groups.
Conclusions: Pts implanted with a TL have a significantly better functional improvement after CRT compared to pts implanted with an EL. Nevertheless long term event-free survival rate do not differ between the two groups.



1136-271 QRS Duration Does Not Predict Ventricular Synchrony-A Tissue Doppler Imaging Study

Shrikanth P. Upadya, Craig McPherson, Sheikh Mahfuzul Hoq, Jeffrey Banker, Prince Mudagol, Gilead Lancaster, Stuart Zarich, Yale University School of Medicine, Bridgeport, CT

Background: Patients (pts) with QRS duration ≤ 120 ms are excluded from cardiac resynchronization therapy (CRT) and as many as a third with QRS > 120 ms fail to benefit from it. Pulsed Doppler tissue imaging (PDTI) may better identify ventricular dyssynchrony and thus pts who may benefit from CRT.
Methods: We correlated QRS duration with the following indices of ventricular synchrony as measured by PDTI: 1) Intraventricular delay (LVD) = differences in electro-mechanical systolic delay in the lateral, septal, anterior, inferior and posterior LV walls (abnormal: >40 ms); 2) Interventricular delay (RLVD) = difference between the RV free wall and the most delayed LV free wall (abnormal: > 40 ms); and 3) Sum dyssynchrony (Sum D) = LVD + RLVD (abnormal: >100 ms).
Results: Among 20 pts (15 men, 17 with ischemic cardiomyopathy, mean age = 70 years), the LVEF was 33 ± 8% in 10 pts with QRS > 120 ms and 25 ± 10% in those with QRS ≤ 120 (p=0.07). The PDTI indices did not distinguish those with QRS > 120 from pts with QRS ≤ 120 (LVD = 130 ± 137 ms vs. 63 ± 30 ms; RLVD = 97 ± 127 ms vs. 57 ± 25 ms; Sum D = 196 ± 255 ms vs. 119 ms ± 54 ms; p=NS for all). LVD was abnormal in 5(50%) pts with QRS ≤ 120, and 7(70%) with QRS > 120.
Conclusions: QRS duration does not correlate with PDTI measures of ventricular synchrony, both under and overestimating dyssynchrony. Thus, PDTI may be the superior method by which to select pts who will benefit from CRT.



1136-272 Cardiac Resynchronization Therapy Improves Left Ventricular Diastolic Function in Non-ischemic Heart Failure

Alan D. Waggoner, Mitchell N. Faddis, Marye J. Gleva, Lisa de las Fuentes, Sharon Heuerman, Victor G, Davila-Roman, Washington University, St. Louis, MO

Background: Cardiac resynchronization therapy (CRT) decreases left ventricular (LV) volumes and improves ejection fraction in patients with heart failure. The effects of CRT on LV diastolic function in patients with ischemic versus non-ischemic etiology have not been well characterized.
Methods: 52 patients [age 61 ± 12 years, 38 males, LV ejection fraction: 25 ± 5%, ischemic etiology in 16 (31%)] were studied prior to, and 4 ± 1 months after CRT. Two dimensional and pulsed-wave Doppler (PWD) echocardiographic measurements included: LV volumes and ejection fraction (EF), mitral E- and A-wave peak velocities, E/A ratio, deceleration time (DT), and diastolic filling time (DFT). Tissue Doppler imaging early diastolic (Em) mitral annular (septal) and color M-Mode flow propagation (FP) velocities were measured in the apical 4 chamber view; PWD E-wave/Em and E/FP were calculated to estimate LV filling pressure.
Results:

	Ischemic (n = 16)		Non-ischemic (n = 36)	
Variable	**Pre-CRT**	**Post-CRT**	**Pre-CRT**	**Post-CRT**
EDV (ml)	221 ± 68	193 ± 63	245 ± 101	211 ± 95*
ESV (ml)	172 ± 59	136 ± 56*	184 ± 86	146 ± 87*
LVEF (%)	23 ± 5	32 ± 10*	26 ± 5	34 ± 11*
E/A	2.3 ± 1.5	1.8 ± 1.3	1.1 ± 0.8	0.8 ± 0.3*
DT (ms)	178 ± 90	177 ± 47	193 ± 58	217±57*
DFT (ms)	351 ± 103	427 ± 113*	352 ± 105	399±126*
E/Em	15.7 ± 5.6	14.3 ± 6.0	13.3 ± 6.9	10.8±5.2*
E/FP	2.4 ± 0.6	2.1 ± 0.7	2.2 ± 0.7	1.7±0.7*
Mean ± SD; * p < .05 vs Pre CRT				

Pre-CRT mitral E/A ratio was higher in ischemic patients (p < .001). LV end-systolic volume decreased, and the LV ejection fraction and DFT increased in both groups. Patients with ischemic etiology did not exhibit significant changes in LV end-diastolic volume, mitral E/A ratio, DT, E/Em or E/FP after CRT.
Conclusions: Both ischemic and non-ischemic heart failure patients improve LV systolic performance after CRT. However, LV diastolic function only improves in non-ischemic patients and remains relatively unchanged in those with ischemic etiology.

POSTER SESSION

1137 Electrocardiographic Markers of Ischemic Heart Disease

Tuesday, March 08, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 11:00 a.m.-Noon

1137-247 Prognostic Value Of Heart Rate Variability In Patients With Unstable Angina

Gaetano A. Lanza, Alfonso Sestito, Giulia Angeloni, Domenico Cianflone, Antonio G. Rebuzzi, Filippo Crea, Attilio Maseri, for the "Stratificazione Prognostica dell'Angina Instablile" Investigators, Università Cattolica del Sacro Cuore, Rome, Italy, Università Vita e Salute, Milan, Italy

Previous studies showed that a reduced heart rate variability (HRV) is of prognostic value in patients with an acute myocardial infarction. Despite the recent interest in risk stratification of patients with unstable angina (UA), the prognostic relevance of HRV in UA patients remains poorly known.
We analyzed Holter ECG recordings of 583 UA patients (63±10 years, 356 men) who underwent 24-hour Holter monitoring within 24 hours from hospital admission. HRV was assessed in the time-domain and in the frequency domain.

During 6-month follow-up, there were 32 total deaths (6.5%). With regard to HRV variables, patients were dichotomized into those with values in the bottom quartile and those with values in the 3 upper quartiles. Low quartile values of most HRV variables were significantly associated with increased mortality at univariate Cox regression analysis (Table). On multivariate Cox regression analysis, including several known prognostic variables (age, gender, cardiac risk factors, type of UA, previous myocardial infarction, ventricular arrhythmias, C-reactive protein and troponin I) reduced low frquency (LF) value was independently associated with both total (RR=2.32, 95% CL=1.1-4.63, p=0.03) and cardiac (RR=3.60, 95% CL=1.1-12.0, p=0.04) death.

	Relative risk (95% C.L.)	P
RR interval <833 ms	2.06 (1.02-4.18)	0.044
SDNN <80 ms	1.56 (0.75-3.24)	0.23
SDANN <62 ms	1.84 (0.90-3.74)	0.09
SDNNi <39 ms	3.00 (1.50-5.99)	0.002
VLF <31 ms	3.07 (1.53-6.14)	0.002
LF <15.7 ms	3.09 (1.54-6.17)	0.001
HF <11.2 ms	1.80 (0.88-3.69)	0.11
LF/HF <1.12	3.57 (1.78-7.15)	0.0003

Thus our data show, for the first time, that decreased HRV is associated with increased mortality at 6-month follow-up in patients with UA, and therefore it can be helpful in risk stratification in this clinical setting.

1137-248 Left Ventricular Ejection Fraction Can Be Derived From Simple ECG Measurements

Patrick R. Krake, Louisiana State University Health Sciences Center, Shreveport, LA

Background: During a non-ST elevation myocardial infarction (NSTEMI) or unstable angina (USA), rapid referral to an early invasive strategy has the greatest benefit to patients with a depressed left ventricular systolic function. Does a reliable, cost effective and universally available source of information to determine the single most important cardiac prognostic factor, left ventricular systolic function, exist? Perhaps a simple tool of clinical medicine that satisfies those important criteria is the surface 12 lead electrocardiogram.
Methods: The study population included 399 consecutive patients who presented to the echocardiography lab, 254 African-Americans and 145 Caucasians, of which 219 were females and 180 were males. The data that was collected from a standard 12 lead surface ECG was summation of the positive and negative forces (R wave + S wave) in lead aVR (aVR) in millimeters. The data from the M-Mode echocardiogram was the left ventricular ejection fraction (LVEF) in percent. Age in years was obtained from the medical record.
Results: With an age adjustment, the simple linear regression model is clearly predictive of LVEF. F ratio is 1916.3 (p<0.001). Squared multiple R: 0.906
$LVEF=\beta_1 aVR + \beta_2 Age$
$\beta_1 = 2.264$, SE = 0.185, T = 12.2, (p<0.001)
$\beta_2 = 0.645$, SE = 0.033, T = 19.7, (p<0.001)
Therefore, a 50 year old with aVR = 10 mm would be expected to have a LVEF of 54.9 %
Conclusion: Numerous studies have repeatedly demonstrated the importance of LVEF. A rapid, reliable and readily available estimation method of LVEF is crucial in the management of the vast majority of cardiac patients. Early risk stratification based on LVEF can determine the urgency of invasive heart catheterization in NSTEMI or USA. In this gender robust and ethnically diverse population, by utilizing a simple arithmetic operation (R wave + S wave) in lead aVR and adjusting for age, the care of the cardiac patient can be optimized based on LVEF. This simple yet effective model has the additional utility secondary to the universal availability, cost effectiveness and ease of interpretation of the surface 12 lead ECG.

1137-249 Association Between Resting Electrocardiographic Parameters and Estimated 10-Year Risk for Coronary Heart Disease in U.S. Population

Hee-Yeol Kim, Don D. Sin, Jae-Hyung Kim, The Catholic University of Korea, Seoul, South Korea, University of British Columbia, Vancouver, BC, Canada

Background: Little is known about the association between parameters in resting electrocardiogram (ECG) and incident coronary heart disease (CHD). We sought to establish the association between ECG and estimated 10-year risk for CHD to analyze whether ECG analysis may yield information that is independent from and additive to traditional risk factors. **Methods**: We applied the risk prediction algorithm used by the National Cholesterol Education Program Adult Treatment Panel III guidelines to data from 6,399 participants (age 40 to 79 years) who had sinus rhythm, no previous heart disease, and no 12-lead Minnesota Code evidence of prior myocardial infarction in the Third National Health and Nutrition Examination Survey. **Results**: After adjusting for age, sex, race and BMI, subjects with high risk had higher levels of heart rate, LV mass index and cardiac infarction injury score, and longer intervals of PR, QRS and heart rate-corrected QT (QTc) than those of low risk. In fully adjusted models for coronary risk factors, participants with high risk were more likely to have upper quintiles of HR and QTc interval, and lower quintiles of PR interval than the controls (Table). **Conclusions**: These findings indicate that long QTc interval, high HR and short PR interval independently predict subjects with high risk for CHD. This suggests that the assessment of ECG parameters may potentially yield information that is additive to the analysis of traditional risk factors in a general population.

Relative odds of having upper quintiles of ECG parameters in subjects with high risk

Variables	Age-, race-, sex-adjusted	*P* value	Age-, race-, sex-, and coronary risk factors-adjusted	*P* value
Heart rate, beats per minute				
Q4, 71-77	1.68(1.30-2.18)	<0.0001	1.65(1.22-2.22)	0.001
Q5, 78-	2.67(2.09-3.42)	<0.0001	2.20(1.65-2.92)	<0.0001
PR interval, msec				
Q4, 168-182	0.81(0.62-1.04)	0.101	0.53(0.39-0.71)	<0.0001
Q5, 183-	0.98(0.76-1.27)	0.894	0.70(0.52-0.94)	0.019
QTc interval, msec				
Q4, 436-450	1.81(1.39-2.38)	<0.0001	1.26(0.92-1.71)	0.149
Q5, 451-	3.10(2.38-4.05)	<0.0001	1.75(1.29-2.37)	<0.0001

1137-250 Do Q Waves on Electrocardiography Predict Non-Viable Myocardium After Acute Myocardial Infarction

Anil Kumar Taneja, Jonathan Swinburn, Bilal Iqbal, Mohammed Khan, Roxy Senior, Northwick Park Hospital, Harrow, United Kingdom

Background: Controversy exists regarding the significance of pathological Q waves on electrocardiography (ECG) after established acute myocardial infarction (AMI) in predicting non-viable myocardium. Dobutamine stress echocardiography (DSE) is now widely used to assess viable myocardium after AMI.
Aim: The aim of the study is to ascertain the reliability of Q waves on the ECG to predict myocardial viability after AMI.
Methods: Accordingly, 178 patients who underwent both ECG and DSE, at a mean of 4.9 days post AMI were assessed.. Non-viability on ECG is defined as the presence of pathological Q waves in at least 4 out of the 6 precordial leads or Q waves in all 3 of the inferior leads. Non-viability on DSE is defined as absence of contractile response in 7 out of the 9-anteroseptal segments or in 3 out of the 4 inferior region segments.
Results: Of the 178 patients, 45% (80) presented with anterior and 44% (78) with inferior AMI. The positive and negative predictive value of Q waves on ECG to predict non-viable myocardium is 24% and 90% respectively. The predictive accuracy was similar in both anterior (84%) and inferior (77%) Q waves.
Conclusion: The presence of extensive Q waves does not predict non-viable myocardium. However, absence of Q waves predicts the presence of viable myocardium.

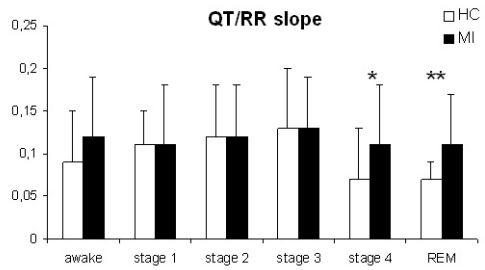
Relationship Between Viability Detected by ECG and that by DSE

	DSE Viability	DSE Non-Viability
ECG Viability	270	31
ECG Non-Viability	42	13

1137-251 QT-Dynamicity During Specific Sleep Stages in the Subacute Phase of Myocardial Infarction

Jana Noethges, Benina Majunke, Jasmin Ortak, Uwe K. Wiegand, Heribert Schunkert, Hendrik Bonnemeier, University Luebeck, Luebeck, Germany

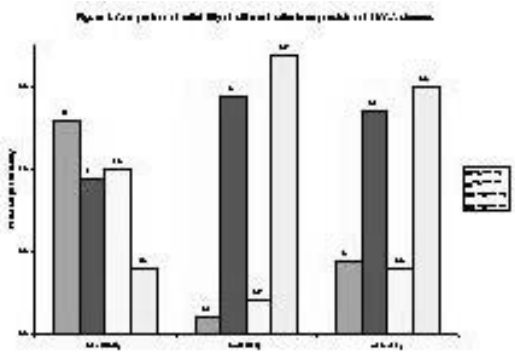
BACKGROUND: Even though sudden cardiac death after myocardial infarction (MI) frequently occur at nightime, the impact of sleep on arrhythmogenesis in patients after MI is yet unknown. We therefore examined the effects of sleep stages on QT-dynamicity and tested the hypothesis that there is a differential effect of sleep stage on the QT/RR relationship in patients with a recent MI compared with healthy controls (HC).
METHODS: Twenty five male patients in the subacute phase of a first uncomplicated MI and 10 healthy age-matched male volunteers without evidence of coronary artery disease underwent polysomnography and simultaneous ECG-recordings. Parameters of QT-interval and QT-dynamicity were measured during wakefulness, sleep stages 1 to 4 of non-REM sleep and during REM-sleep.
RESULTS: QT- and RR-interval increased through all sleep stages in both, MI-patients and HC. The Bazett-corrected QTc-interval remained stable from wakefulness through all sleep stages. QT/RR-slopes remained stable from wakefulness to sleep stage 3 in both groups, however, in contrast to MI-patients there was a significant decrease during deep-sleep and REM-sleep in HC. QT/RR-slopes were significantly steeper in MI-patients during these sleep stages.
CONCLUSION: MI causes an abnormal QT/RR relationship in deep sleep and REM-sleep, reflecting an inadequate shortening of repolarization with increasing heart rate, which may have important implications for sleep-selected ventricular arrhythmias after MI.



1137-252 ECG Predictors Of Left Main Coronary Artery Obstruction: ST Segment Deviation In Lead V6 Greater Than Or Equal To ST Segment Deviation In Lead V1.

Nitin Mahajan, Deepak Thekkoott, Brian Temple, Bilal Malik, Sunil Abrol, David Yens, Malcolm Rose, Jacob Shani, Edgar Lichstein, Gerald Hollander, Maimonides Medical Center, Brooklyn, NY

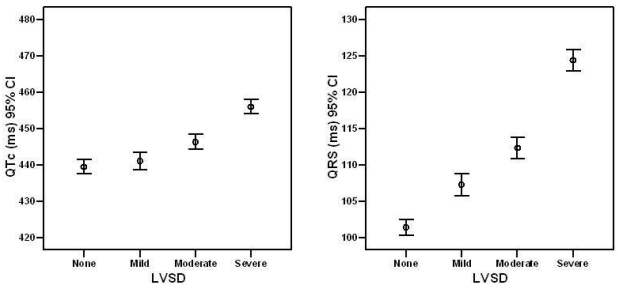
Background: Acute Coronary Syndrome (ACS) resulting from culprit lesion in left main coronary artery (LMCA) can cause rapid hemodynamic deterioration. It is important to identify these patients early to facilitate timely revascularization. ST segment elevation in aVR greater than or equal to V1 (aVR-V1≥0) has been suggested as a sensitive predictor of LMCA disease. As a result of balanced forces, we hypothesized that ST deviation in V6 greater than or equal to ST deviation in V1 (V6-V1≥0) might be a good determinant of LMCA disease.
Methods: We compared admission 12-lead ECGs of ACS resulting from culprit LMCA lesion (n=75:Group I) with ACS resulting from culprit left anterior descending artery (n=81:Group II). Group I was selected over a period of 10 years. We compared V6-V1≥0 to aVR-V1≥0 in both groups. We also looked at ratio of ST deviations in V6,V1 (V6/V1≥1) and aVR,V1 (aVR/V1≥1) in cases where ST segment in V1 was not isoelectric(GpI-54/75: GpII-55/81).
Results: In group I, ST deviation in V6 was significantly greater than ST deviation in V1 (0.06, t=10.44,p<0.01). Figure 1 demonstrates the reliability of V6-V1≥0, V6/V1 ≥1, aVR-V1≥0 and aVR/V1≥1 in predicting LMCA disease.
Conclusion: This is the largest series on ECG analysis on ACS resulting from culprit LMCA lesion. V6-V1≥0 is more sensitive in predicting LMCA as culprit vessel than previously reported aVR-V1≥0.



1137-253 Relationship between Severity of Heart Failure and Repolarisation Abnormalities on the Surface ECG - Euro Heart Failure survey.

Periaswamy Velavan, Nasrin K. Khan, Alan S. Rigby, Michel Komajda, Ferenc Follath, Karl Swedberg, Andrew L. Clark, John G F Cleland, University of Hull, Hull, United Kingdom

Introduction: QT prolongation predicts arrhythmic events and indicates poor prognosis in heart failure. It is associated with increased risk of coronary disease and cardiovascular mortality.
Hypothesis: QT interval is prolonged in left ventricular systolic dysfunction (LVSD) and is linearly related to its severity.
Methods: From the EURO-HF survey, the QT, QTc, QRS and JT intervals were measured from 5829 ECGs with a digital caliper and related to LV function, assessed by echocardiography.
Mean age was 69 ± 13 years; 41% were women; 64% had coronary disease; 54% had hypertension; 27% had diabetes and 18% had renal dysfunction.
Results: QT, QTc and QRS intervals were prolonged in LVSD and were related to its severity. The odds ratio for having moderate or severe LVSD increased with increasing QRS interval with a dose response effect: QRS 120-140 ms, OR **2.7**; 141-160 ms, OR **3.4**; 161-180 ms, OR **3.9** and >180 ms, OR **4.6** (p=<0.0001). But there was no such effect seen with QTc interval: QTc 440-460 ms, OR **1.1**; 461-480 ms, OR **1.3**; 481-500 ms, OR **1.2** and >500 ms, OR **1.0** (p=0.379).
Conclusions: QTc, QT and QRS intervals are prolonged in patients with LV systolic dysfunction and are related to its severity. The QT prolongation is mainly influenced by the increase in the QRS interval and probably reflects the severity of LV dysfunction in patients with heart failure rather than representing abnormal repolarisation.



1137-254 Inaccuracy of the Minnesota Code for Recognition of Prior Myocardial Infarction

Sangeeta Shah, Frederico Asch, Anthon Fuisz, Ellen Pinnow, Joseph Lindsay, Washington Hospital Center, Washington, DC

Background: The ECG is valuable in epidemiological studies and in screening examinations for the identification of prior MI. The Minnesota Code (MC), commonly used in such settings, provides criteria for the identification of prior MI. Their accuracy is, however, unclear. We tested the MC Q and QS criteria for prior MI against a novel standard, the presence of myocardial scar as represented by delayed hyper-enhancement on magnetic resonance imaging (MRI).
Methods: Delayed hyper-enhancement of the myocardium after gadolinium injection was sought in 146 consecutive pts undergoing cardiac MRI. Most were examined to assess myocardial viability. 139 had ECG's within 2 weeks. A physician, blinded to the ECG, assessed volume, location and transmural extent of scar. Two experienced cardiologists read the ECGs utilizing MC Q and QS criteria.
Results: 66 (47.5%) pts had delayed hyper-enhancement. 32 (48.5%) had Q or QS criteria. Sensitivity was affected by the size of scar but not independently by location. Of 26 pts with a scar ≥20% of left ventricular volume, 17 (65.4%) had MC criteria as compared to15 of 40 (37.5%) with a smaller scar. In 63 (95.5%) pts scar involved ≥75% of the wall thickness. Of them, 31 (49.2%) had MC criteria for MI. Of 73 pts without delayed hyper-enhancement, 12 (16.4%) had Q or QS criteria for MI.
Conclusions: When compared to the presence of myocardial scar as assessed by delayed hyper-enhancement, MC Q and QS criteria for MI have a sensitivity of approximately 50%. Scars ≥20% of LV volume were more often detected (65.4%) than those <20% (37.5%). MC criteria were found in 16.4% of pts with no scar. (specificity of 83.6%) Thus, in a population undergoing viability testing by MRI, MC code criteria are relatively insensitive, particularly for small scar, and less than ideally specific for the detection of prior MI.

1137-255 ST Segment Vector in ST Segment Elevation Myocardial Infarction Involving the Left Circumflex Artery

David N. Kenigsberg, Mouaz Al-Mallah, Mark E. Josephson, Subramaniam C. Krishnan, Sanjaya Khanal, Henry Ford Hospital, Detroit, MI, Beth Israel Deaconess Medical Center, Boston, MA

Background: The pattern of ST segment elevation (STE) in inferior myocardial infarction (IMI) is useful in predicting the culprit vessel. When the culprit is the right coronary artery, the ST segment vector is directed inferiorly and to the right, resulting in STE in lead III greater than II (III>II). Conversely, when the culprit is the circumflex artery (LCx), the ST vector is directed inferiorly and to the left, resulting in STE in lead II greater than III (II>III). This concept has not been well validated, especially in LCx infarcts. We examined the distribution of ST segment changes in the inferior (II,III,aVF), lateral (I,aVL) and early precordial leads (V1-V3) in patients with STE IMI where the culprit vessel was the LCx.
Methods: Using our catheterization laboratory database (1988-2003), of 370 patients undergoing angioplasty for IMI, 71 patients were identified where the culprit was the LCx . Of these, 49 had inferior STE on ECG.
Results: STE II>III was present in 12/49 (25%) of patients. These patients were more likely (58%) to have STE in I or aVL (p=0.0002). Posterior injury, defined as STD V1-V3, was seen in 83% of this group (p=0.08). 17/49 patients (34.7%) had STE in III not greater than II. STE III>II was present in 21/49 (43%) of patients. They were more likely (76%) to have STD in I and/or aVL (p=0.01).

STE (n,%)	STE I or aVL	STD I or aVL	Posterior Injury (STD V1-V3)	ST Segment Vector	RCA Dominance
II>III (12,25)	7 (58%)	2 (17%)	10 (83%)	Inferior, Right to Left	11 (91%)
II not > III (17,35)	1 (6%)	6 (35%)	10 (59%)	Inferior	10 (59%)
III>II (21,43)	1 (5%)	16 (76%)	12 (57%)	Inferior, Left to Right	17 (81%)

Conclusion: In STE IMI due to LCx occlusion, only a minority (25%) of patients have the ST segment vector directed inferiorly and to the left (STE in II>III); of these, 58% have STE in I and/or aVL.

1137-256 Repolarization Duration in Postinfarction Patients with Conduction Disturbances

Katarzyna Piotrowicz, Wojciech Zareba, Scott McNitt, Arthur J. Moss, University of Rochester, Rochester, NY

The aim of the study was to compare different measures of repolarization duration in postinfarction patients with and without conduction disturbances and to evaluate the prognostic significance of repolarization parameters for predicting mortality in patients with conduction abnormalities (LBBB,RBBB, IVCD).
Methods: Study population consisted of 3,282 pts after recent MI (mean age 57 years). Repolarization duration was measured using QTc_B (Bazett corrected QTc), JTc (Bazett corrected QTc after subtracting QRS complex duration), and JT_{RR} (formula by Rautaharju: JT_{RR}=JT-155(60/HR-1)+k; k=34ms for male; 22ms for female).
Results: Table below shows mean±sd values of repolarization parameters in respective subgroups. QTc_B in LBBB patients demonstrate excessive prolongation of repolarization, which could not be documented when using JT_{RR}. There was 29% 2-year mortality in 363 patients with conduction abnormalities. After adjustment for significant clinical predictors (age, EF, NYHA class) of mortality, hazard ratios for variables dichotomized at 75th %-ile were: for JTc>360 = 1.31 (p=0.23), for JT_{RR} >362 ms = 1.59 (p=0.027), and for QTc>480ms = 1.51 (p=0.055).
Conclusion: 1) Patients with LBBB, RBBB, IVCD show longer QTc than patients without these conduction disturbances. JT_{RR} reflects better than QTc repolarization duration in patients with conduction disturbances. 2) JT_{RR} significantly and independently predicts mortality in postinfarction patients with conduction disturbances.

* p<0.001 for comparison with normal conduction

	Normal Conduction N=2919	IVCD N=185	RBBB N=131	LBBB N=47
QRS (ms)	82 ± 9	111± 12*	128 ± 14*	138 ± 15*
QTc_B (ms)	415 ± 37	445 ± 40*	452 ± 45*	495 ± 56*
JTc (ms)	333 ± 37	334 ± 50	325 ± 46	358 ± 40*
JT_{BB}	350 ± 30	345 ± 38	335 ± 37*	355 ± 39
QT_c>440(%)	22	52	60	85
JT_{BB}>37(%)	24	20	11	34

ORAL CONTRIBUTIONS

847 Techniques and Outcomes of Atrial Fibrillation Ablation

Tuesday, March 08, 2005, 10:30 a.m.-Noon
Orange County Convention Center, Room 232A

10:30 a.m.

847-3 Comparative Evaluation of Platelet and Coagulation Activation During Transvenous Cryoablation and Radiofrequency Ablation for Pulmonary Vein Ablation in Patients with Atrial Fibrillation

Hung Fat Tse, Yok-Lam Kwong, Chu-Pak Lau, Department of Medicine, Queen Mary Hospital, University of Hong Kong, Hong Kong, Hong Kong

Background. The potential thromboembolic risk associated with radiofrequency ablation (RF) of pulmonary veins (PV) raises the question of whether use of cryoablation (Cryo) would provide a safer profile. The aim of this study was to compare the thrombogenic potential of Cryo with RF ablation during PV ablation.
Methods and Results. 30 patients (52±3 yrs, 23 M) with paroxysmal atrial fibrillation were randomised to undergo PV isolation using either 4mm-tip RF (n=15) or Cryo (CryoCor, CA) (n=15). Blood samples were drawn to assess platelet (Plt) and coagulation (CA) activation at baseline, after transeptal puncture (TS), before ablation and after successful isolation of a superior PV. After TS, heparin was given to keep ACT>250s. Plt activation was assessed by flow cytometry of P-selectin. CA activation was measured by ELISA assay of plasma level of prothrombin fragment 1+2 (F1+2) and thrombin-antithrombin III complex (TAT). Both Plt and CA activation were signifiantly increased after TS (Fig. A & B). The percentage changes in Plt activation from baseline were significantly lower after Cryo compared to RF (Fig. A). However, there were no significant differences in CA activation between RF and Cryo, with both of them decreasing after heparin (Fig B). **Conclusions.** Significant Plt and CA activation were observed during PV isolation procedure. The use of Cryo was associated with a significantly lower Plt activation compared to RF, suggesting potentially lower thrombogenic risk during PV isolation procedure.

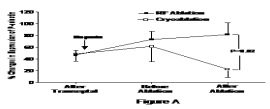


Figure A

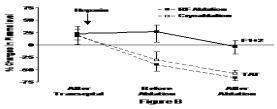


Figure B

10:45 a.m.

847-4 Acute Efficacy and Midterm Follow-up in Patients Treated by Circumferential Ostial Cryoisolation of Pulmonary Veins

Juergen Vogt, Johannes Heintze, Helga Buschler, Peter Schwartze, Dieter Horstkotte, Heart Center North Rhine-Westphalia, Ruhr University Bochum, Bad Oeynhausen, Germany

Background: Segmental isolation of pulmonary veins (PV) with radiofrequency (RF) ablation is associated with reconducting muscle sleeves and the risk of PV stenoses. This study reports on the efficacy of circumferential PV isolation using the new Arctic Circler (AC) (Cryocath, Canada).
Methods: Guided by a Lasso catheter before and after ablation, proximal PV isolation was performed using the up to 30 mm self-expanding AC over 4 minutes of cryoimpulses (CI) down to -85°C with N_2O. Gaps were closed using a 6-/8-mm tip cryocatheter (Freezor xtra/max).
Results: 41 P (9 women, age 59±9 years, 38 with paroxysmal, 3 with persistent atrial fibrillation (AF), 21 with lone AF, 12 with hypertension, 7 with CAD, 1 with mitral valve disease) were treated with the AC. 13 of 155 PV were isolated with 6 mm tip only. 142 PV (100%) were isolated, with AC alone in 44 % (62 PV) with additional gap closing in 56% (79 PV). During a follow-up of 8±4 months of 30 P after 1.4 procedures per P, 13 (43%) had no recurrence, 9 (30%) had a marked reduction of AF burden, i.e. an overall clinical improvement of 74%. 3 of 7 P without improvement had persistent AF. In 13 redos 43% (22 PV) of 51 PV were completely isolated (12 PV) or demonstrated 1-2 local inputs (10 PV) only. Excluding persistent AF, the clinical success was 81%.
Conclusion: The combination of circumferential ostial PV isolation and gap closing with cryotechnique is highly effective. More cooling power is necessary to reduce PV reconduction. The risk of PV stenosis seems to be eliminated.

Targeted PV	Diameter (mm)	Isolation AC	Freezor only	Isolation AC + Freezor	Isolation % total	Cryoimp AC	Cryoimp Freezor
left upper (n=41)	18±4	12 (29%)	1	28	100	5±2	6±4
left lower (n=36)	17±2	18 (50%)	5	13	100	3±1	5±2
right upper (n=41)	18±3	16 (39%)	3	22	100	4±1	5±4
right lower (n=34)	16±3	16 (47%)	4	14	100	3±1	4±3
right mid (n=3)		1		2	100		

11:00 a.m.

847-5 Symptomatic and Asymptomatic Atrial Fibrillation in Patients Undergoing Radiofrequency Catheter Ablation

Chandrasekhar R. Vasamreddy, Darshan Dalal, Vinod Jayam, Zayd Eldadah, Timm Dickfeld, Jun Dong, Charles Henrickson, Glenn Meininger, Ronald Berger, Hugh Calkins, Johns Hopkins School of Medicine, Baltimore, MD

Background: The goals of this study are 1) to report the relationship between symptoms and atrial fibrillation (AF), and 2) to report the efficacy of catheter ablation procedure based on patient reported symptoms compared to the efficacy based on monitoring systems that can detect both symptomatic and asymptomatic AF recurrences.
Methods: 19 consecutive patients (12 men [63%]; age 60 ± 6 years) with highly symptomatic drug refractory paroxysmal (6 patients [32%]), persistent (6 patients [32%]) or permanent (7 patients [38%]) AF underwent catheter ablation using the circumferential approach described by Pappone and colleagues. Patients were provided with mobile cardiac outpatient telemetry systems (MCOT) (CardioNet, USA) monitors and asked to wear it 5 days immediately before the ablation, and 5 days per month starting with the ablation for 6 consecutive months. When patients experienced any symptoms, they were asked to activate the system and asked to select one or more of the following symptoms: skipped beats, lightheadedness, fainting, shortness of breath, chest discomfort, fatigue, heart racing, and palpitations.
Results: A total of 494 days (11,856 hours) were monitored. During this period, 2870 events occurred that were either triggered automatically [2480 (86%)] or by the patient [390(14%)] resulting in transmission of tracing. Of these 885 (31%) events were due to AF [156 (18%) symptomatic and 729 (82%) asymptomatic events]. Out of the total 390 events triggered by patients' symptoms, 40% were confirmed as AF events (156) and 60% were confirmed as non-AF events (234). Out of the symptoms, only shortness of breath (OR: 5; P: 0.008) and chest discomfort (OR: 5; P=0.011) are highly associated with AF. Events with two or more symptoms are also highly associated with AF (OR: 6.7, P= 0.001). At the end of 8 ± 1 months of follow-up, 12 patients (63%) were considered to be free of AF based on the absence of symptomatic AF recurrences whereas 10 patients (53%) have achieved true success when asymptomatic AF recurrences were included in the outcome (p<0.05).
Conclusion: The reliance on patient reported symptoms appears to overestimate the efficacy of catheter ablation of AF.

11:15 a.m.

847-6 Role of the Coronary Sinus in Atrial Arrhythmias Following Left Atrial Circumferential Ablation for Atrial Fibrillation

Aman Chugh, Hakan Oral, Kamala Tamirisa, Jihn Han, Eric Good, Kristina Lemola, Frank Bogun, Frank Pelosi, Jr., Fred Morady, University of Michigan, Ann Arbor, MI

BACKGROUND: The musculature of the coronary sinus (CS) has been implicated in a variety of supraventricular arrhythmias. Its role in arrhythmias following left atrial circumferential ablation for atrial fibrillation (AF) is unknown. **METHODS:** Fourteen patients (Males=10, Age=55±10 years, EF=53±10, LA=4.3±0.5 cm, paroxysmal AF=9) were found to have atrial arrhythmias originating from the CS either during the initial procedure (4) or a repeat procedure for recurrent AF/atypical flutter at follow up (10). A tachycardia was considered to be originating from the CS if the post pacing interval matched the tachycardia cycle length or if the tachycardia terminated during ablation in the coronary sinus or one of its branches.
RESULTS: The mechanism was macroreentry in 13 patients (93%) and focal in one patient. The mean cycle length of the tachycardia in patients with macroreentry was 260±29 ms (range, 190-310 ms). The cycle length of the focal tachycardia was 725 ms. The successful site was the proximal CS in 6 patients (43%) and distal CS in 8 patients (57%). Catheter ablation was successful in 13 patients (93%). Ablation was not performed in one patient because of high impedance. In six patients (43%), ≥45 W and >50° C were required for successful ablation. There were no complications.
CONCLUSIONS: The musculature of the CS may serve as a site for macroreentrant atypical flutter or focal atrial tachycardia following linear left atrial ablation for AF. Catheter ablation of these arrhythmias seems to be safe and effective. Although low power and temperature settings are usually recommended during radiofrequency application in the CS, a number of patients required significantly higher energy delivery for successful ablation.

11:30 a.m.

847-7 Segmental Disconnection and Tissue Anisotropy at the Human Pulmonary Vein-Atrial Junction: Implications for Catheter Ablation of Atrial Fibrillation

Alex Y. Tan, Hongmei Li, Peng-Sheng Chen, Michael C. Fishbein, Cedars-Sinai Medical Center, Los Angeles, CA, David Geffen School of Medicine, UCLA, Los Angeles, CA

Background: We previously showed that in canines, pulmonary vein (PV) and left atrial (LA) muscle are disconnected preferentially in the anterior compared to posterior segments. This arrangement suggests that the posterior PV-LA junction may serve as the

preferred ablation target in PV-LA electrical disconnection, if this segmental variation is also present in the human PV-LA junction.
Methods: Paraffin embedded sections of PVs and adjoining LA were obtained from 7 adult human hearts at postmortem (age 54 ± 17 years). None had AF, structural heart disease or died of cardiac causes. Each vein was sectioned along its long axis into 6 segments (3 anterior, 3 posterior) and stained with hematoxylin and eosin and Masson's trichrome. Analysis was performed in blinded fashion with the aid of computer-assisted morphometry.
Results: Out of 168 sections from 28 veins, partial or complete PV-LA disconnection was observed in 74 sections (44%), more commonly in the anterior vs posterior junction (55 vs 19, p<0.001). The gap between PV and LA muscle was 0.4 ± 0.23mm. LA to PV transition was marked by abrupt reduction of muscle sleeve thickness more prominent in the anterior vs posterior junction (by 75 ± 12% vs 52 ± 17%, P=0.003). Fiber orientation was more complex at the PV-LA junction than in the LA or distal PV, with 41 (24%) PV-LA junctions showing abrupt 90-degree fiber direction changes from perpendicular to parallel or vice-versa. This finding was more common in the anterior vs the posterior junction (30 vs 11, p<0.001).
Conclusions: Segmental disconnection of PV and LA is more common and fiber orientation changes more pronounced in the anterior than posterior PV/LA junction. This anisotropy would favor impulse propagation in the posterior junction and suggests that catheter ablation targeting the posterior junction may be most efficacious in disconnecting PV from LA in the treatment of atrial fibrillation.

11:45 a.m.

847-8 Catheter Ablation for Persistent and Permanent Atrial fibrillation: Left Atrial Ablation Alone Versus Biatrial Ablation

Leonardo Calo', Filippo Lamberti, Maria Luisa Loricchio, Ermenegildo de Ruvo, Claudio Pandozi, Massimo Santini, San Filippo Neri Hospital, Rome, Italy

Background: Catheter ablation of atrial fibrillation (AF) has a low efficacy in patients (pts) with persistent and permanent AF.
Methods: Sixty patients with persistent (35 pts) and permanent AF (25 pts) highly symptomatic and refractory to anti-arrhythmic drugs (AAD) (22 women, 59± 9 yrs, 48 pts with structural heart disease) were prospectively randomized to 2 different ablation approaches guided by CARTO mapping. Thirty pts underwent to circumferential pulmonary vein (PV) ablation and cavotricuspid isthmus ablation (approach A). In the other 30 pts the following lesions were added in the right atrium (approach B): 1) Intercaval posterior line; 2) Intercaval septal line through the fossa ovalis and the coronary sinus where a circumferential line around the ostium was performed; 3) Electrical disconnection of the superior vena cava. The clinical characteristics of the pts in the 2 groups were similar. All pts continued previously ineffective AAD for at least 6 months.
Results: During a mean follow-up of 12 ± 4 months, 63% of patients (19/30) who underwent left atrial and cavo-tricuspid ablation were AF free compared with 87% of patients (26/30) who underwent biatrial ablation (p=0,039, log rank test). Post-ablation re-mapping showed the absence of discrete electrical activity inside and just around ablation lines both in the left and in the right atrium. The mean duration of procedure and fluoroscopy times for the approach A were 165±26 and 30±10 minutes, and for the approach B were 226±30 and 40±13 minutes. An hemothorax and a retroperitoneal hematoma occurred in 2 pts of the left atrial ablation group. During the follow-up left atrial flutter, which resolved spontaneously, developed in 3 pts.
Conclusion: Our biatrial approach showed to be feasible, safe and effective to modify the right and left AF substrate. This study first demonstrates that in pts with persistent and permanent AF the circumferential PV ablation in combination with linear lesions in the right atrium determines a significant higher success rate than circumferential PV ablation and cavo-tricuspid isthmus ablation alone. These preliminary data need to be confirmed in a randomized trial with larger population and longer follow-up.

POSTER SESSION

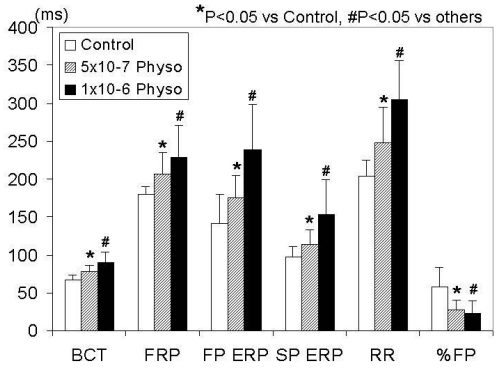
1163 Clinical and Basic Insights Into the Mechanisms of Atrial and Ventricular Fibrillation

Tuesday, March 08, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 3:30 p.m.-4:30 p.m.

1163-253 Enhanced Vagal Tone Has Disparate Effects on Atrioventricular Node Dual Pathway Electrophysiology During Atrial Fibrillation

Youhua Zhang, Seil Oh, Todor N. Mazgalev, Cleveland Clinic Foundation, Cleveland, OH

Background: The effects of enhanced vagal tone on atrioventricular node (AVN) dual pathway electrophysiology, especially during atrial fibrillation (AF), is not clear. We used a novel index, His electrogram alternans (*Circulation* 2003;107:1059), to monitor the fast (FP) and slow pathway (SP) conduction on a beat-by-beat basis during AF in response to enhanced vagal tone.
Methods: Physostigmine (an acetylcholinesterase inhibitor) was used to enhance the vagal tone in 5 rabbit AVN preparations. Standard AVN conduction curves were generated by programmed stimulation and 500 RR intervals were collected during pace-induced AF, in control and after perfusion with Physostigmine ($5x10^{-7}$M to $1x10^{-6}$M). Atropine ($2x10^{-6}$M) was added finally to confirm vagal effects.
Results: See figure. Physostigmine increased basic AVN conduction time (BCT) and functional refractory period (FRP) in a dose-dependent manner. The effective refractory periods (ERP) of both pathways were prolonged, but FP-ERP increased more than SP-ERP (ΔFP-ERP=97 ms, vs ΔSP-ERP=57 ms at $1x10^{-6}$M physostigmine, p<0.05). During AF, the average RR intervals prolonged and the proportion of beats conducted via FP (%FP) declined (57% in control, to 23% at $1x10^{-6}$M physostigmine, p<0.05). These effects were abolished by atropine.
Conclusions: Enhanced vagal tone inhibited both FP and SP, but FP was more sensitive than the SP. Under enhanced vagal tone, SP played a dominant role in determining the ventricular rate during AF.



1163-254 Atrial Fibrillation in Humans Is Not Associated With Atrial Sympathetic Hyperinnervation

Paul A. Gould, Michael Yii, Samara Finch, Tanneale Marshall, Flora Socratos, Gavin Lambert, David M. Kaye, Baker Heart Research Institute, Melbourne, Australia, Department of Cardiothoracic Surgery St Vincent's Hospital, Melbourne, Australia

Background: Pacing animal models of atrial fibrillation (AF) have demonstrated sympathetic hyper-innervation of the left and right atrium. We believed this is secondary to pacing and not related to AF. As this finding may have implications for management of AF in humans, we sought to investigate atrial sympathetic innervation in human AF and compare this with sinus rhythm (SR).
Methods: In 24 patients (12 in SR and 12 in AF) undergoing bypass surgery we collected right atrial appendages and also 12 left atrial appendages in AF patients only. We then performed immuno-histochemistal staining for tyrosine hydroxylase (TH) and growth associated protein (GAP43). In addition we performed real time polymerase chain reaction to quantify expression of nerve growth factor (NGF) RNA and measured tissue norepinephrine using high performance liquid chromatography and electrochemical detection.
Results: The amount of TH (AF 0.23 ± 0.1%, SR 0.19 ± 0.07%, p=0.90) and GAP43 (AF 0.83 ± 0.7% , SR 0.69 ± 0.3% , p=0.67) neural staining as assessed by percentage area of 10 fields at 10X magnification using light microscopy was not significantly different between right atria from either AF or SR group. NGF RNA expression (p = 0.81) and tissue norepinephrine content (p= 0.27) were also not significantly different between right atria in SR or AF. However in the AF group, tissue norepinephrine (p<0.001) and TH staining (p= 0.049) were significantly greater in the right atrial appendage compared with the left, implying greater sympathetic innervation on the right.
Conclusion: AF in humans is not associated with sympathetic hyper-innervation. That seen in pacing induced animal AF is likely secondary to pacing. In human AF there is greater sympathetic innervation of the right atrium compared with the left.

1163-255 Nerve Sprouting and a Canine Model of Paroxysmal Atrial Fibrillation

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Background: We hypothesize that the induction of atrial nerve sprouting and sympathetic hyperinnervation in dogs with electrical remodeling may create a model of paroxysmal atrial fibrillation (PAF) and paroxysmal atrial flutter (PAFL).
Methods and Results: We studied 6 dogs (experimental group) with complete heart block, myocardial infarction and sympathetic hyperinnervation induced either by nerve growth factor (NGF) infusion (N=2) or subthreshold electrical stimulation (N=4) of the left stellate ganglion (LSG). Cardiac rhythm was continuously monitored by a Data Sciences International (DSI) transmitter for 43±31 days. Three normal dogs were also monitored to serve as rhythm control. Six additional normal dogs were used for histology control. PAF and PAFL were documented in all dogs of experimental group, with an average of 3.9±3.3 episodes per day including 1.7±1.7 episodes of PAF and 2.2±2.1 episodes of PAFL. The duration averaged 314±648 s (range 7 s - 4000 s). There was a circadian pattern of arrhythmia onset (P<0.01), with the highest incidence in morning and early afternoon. Normal dogs did not have either PAF or PAFL. The hearts from dogs with LSG electrical stimulation had a higher density of nerve structures immunopositive (P<0.01) in both right and left atria than that of control dogs.
Conclusions: Induction of nerve sprouting and sympathetic hyperinnervation in dogs with AV block and myocardial infarction creates a model of PAF and PAFL. The circadian pattern of arrhythmia onset suggests that the sympathetic tone played an important role in the generation of PAF and PAFL.

1163-256 Altered Patterns of Gene Expression in Response to Chronic Atrial Fibrillation

Youngkeun Ahn, Nam Ho Kim, Seok Kyu Oh, Myung Ho Jeong, Jeong Gwan Cho, Byung Hee Ahn, Jong Bum Choi, Hyun Kook, Jong Chun Park, Jin-Won Jeong, Jung Chaee Kang, Chonnam National University Hospital, Gwangju, South Korea

Background: To obtain more insight into atrial remodeling at the molecular level we analyzed the changes in the gene expression in human atrial tissue between the patients with chronic AF and those with normal sinus rhythm (NSR).
Methods: cDNA microarray analysis was used to identify genes differentially expressed during sustained AF of more than 6 months (n=8, mean age=45±12, M:F=2:1) as compared to those with NSR (n=8, mean age=47±13, M:F=2:1). Western blot analysis was performed to confirm the altered gene expressionand to establish the changes in protein expression between those with chronic AF and the NSR group. DNA gel electrophoresis to establish the DNA ladder formation which was associated with apoptosis in response to chronic AF was performed in the chronic AF and NSR groups. Microscopic findings were observed via electron microscopy between the patient with chronic AF and the NSR group.
Results: In the microarray analysis, out of 8,167 candidate genes, 66 genes showed a significant change in the expression level in the patients with chronic AF, which was in contrast to those with NSR. Among those, 31 genes were consistently down-regulated and 35 up-regulated more than 2-fold. The relative amounts of the Bcl-2 and p27 in the atrial tissue were decreased (p=0.017, p=0.014, respectively) and AT2-R and p21 were increased (p=0.035, p=0.045, respectively) in the patients with chronic AF as compared to those with NSR. The atrial cardiomyocytes in chronic AF showed a prominent DNA ladder, which is a biochemical hallmark of apoptosis. An abnormal ultrastructure was seen in the mitochondria, intercalated disks, and sarcomeres in the atrial tissue samples taken from the patients with chronic AF.
Conclusions: The expression of Bcl-2, AT2-R, p21, and p27 was consistent with a significant role in the apoptosis of cardiac myocytes in the patients with chronic AF. Further study on the effect of the drugs which modulate the expression of these proteins in patients with chronic AF will be needed.

1163-257 New Insights into the Atrial Flutter Reentry Circuit - Studies during Entrainment

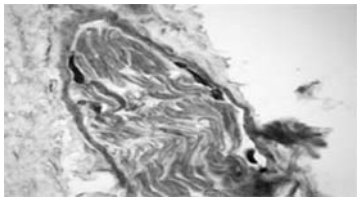
Naomichi Matsumoto, Celeen M. Khrestian, Kyungmoo Ryu, Albert L. Waldo, Case Western Reserve University, Cleveland, OH

Background: Atrial flutter (AFL) due either to single loop or double loop reentry occurs in the canine sterile pericarditis model. We tested the hypothesis that in this model: 1) the cavo-tricuspid (CT) isthmus is a critical part of both types of AFL; 2) an area of slow conduction in the reentrant circuit is always present in the right atrial (RA) free wall, not the CT isthmus.
Methods: Studies were performed 4 days after the creation of sterile pericarditis in 6 dogs. During induced, sustained AFL (> 10 minutes), simultaneous, multisite, epicardial mapping was performed from 404 electrodes placed on both atria in the open chest state together with either a halo electrode catheter (10 pairs) at the tricuspid annulus or a quadripolar catheter at the CT isthmus. Entrainment pacing during AFL was performed from the CT isthmus at cycle lengths (CLs) 5-10 ms less than the AFL CLs. Sites were considered to be within the AFL reentrant circuit when the post pacing interval (PPI) minus AFL CL was ≤ 30 ms. The PPI was defined as the time from the last captured electrogram to the onset of the first post pacing electrogram at a site immediately adjacent to the pacing site. **Results:** During 6 episodes of AFL (mean CL 159±21 ms, range 138-193 ms), 3 single loop reentry circuits and 1 double loop reentry circuit were shown to have the CT isthmus within the AFL reentry circuit (PPI minus AFL CLs were < 20 ms, mean 10±5 ms). In all of these examples, atrial septal activation was part of the reentrant circuit. Mapping and entrainment pacing during the other 2 AFL episodes demonstrated RA free wall reentry without involvement of the CT isthmus in the AFL reentry circuit (PPI minus AFL CLs were > 30 ms, mean 40±14 ms). Also, the PPI was significantly longer than when the CT isthmus was in the circuit ($p < 0.01$). The area of slow conduction was in the RA free wall, and showed increased crowding of isochrones as the pacing CL was decreased during entrainment pacing.
Conclusions: In the canine sterile pericarditis model of AFL, 1) the CT isthmus is not always part of the reentry circuit; 2) the area of slow conduction is always in the RA free wall.

1163-258 Autonomic Innervation of the Pulmonary Veins

Joseph S. Ulphani, Alan Kadish, Firdous Inderyas, David Gordon, Kathleen Harris, Jeffrey Goldberger, Robert Decker, Alexander Morris, Shawana Zahir, Jason Ng, Rishi Arora, Northwestern University, Chicago, IL

BACKGROUND: The autonomic nervous system is believed to play a role in the genesis of focal atrial fibrillation. However, the precise distribution of sympathetic and parasympathetic nerves within the pulmonary veins (PV) has not been systematically described.
METHODS: Serial circumferential cross-sections from normal canine PVs (N=6) were studied. The PV myocardium was immunostained for sympathetic (tyrosine hydroxylase, dopamine beta-hydroxylase) and parasympathetic nerves (acetylcholine esterase, choline acetyltransferase).
RESULTS: Sympathetic and parasympathetic innervation was noted in the PV myocardial sleeves; nerve bundles were mostly localized to the subepicardial aspect of the PVs. Double-staining revealed predominatly parasympathetic nerves within individual nerve bundles. The figure shows parasympathetic staining (brown wavy nerve fibers) and sympathetic staining (dark blue) within a single nerve bundle from a circumferential section at 40X magnification.
CONCLUSIONS: Sympathetic and parasympathetic innervation of the PVs appears to be heterogeneous in nature; this heterogeneity may contribute to the electrophysiologic substrate for focal atrial fibrillation.



1163-259 Sustained Atrial Fibrillation and Enhanced Susceptibility to Ventricular Tachycardia in the Annexin A7-Deficient Mouse

Jan W. Schrickel, Claudia Herr, Christoph S. Clemen, Martina Rick, Christian Grohé, Rainer Meyer, Klaus Tiemann, Rolf Schroeder, Angelika A. Noegel, Berndt Luederitz, Thorsten Lewalter, University of Bonn, Bonn, Germany

Background: Annexin A7 (anxA7) is thought to be involved in membrane organization and Ca^{2+}-dependent signalling processes. In isolated cardiomyocytes of anxA7$^{-/-}$ mice, altered cell shortening frequency relation has been detected and attributed to anxA7 related changes of Ca^{2+} homeostasis. The aim of the present investigation was to evaluate cardiac electrophysiologic properties in anxA7-deficient mice in vivo.
Methods: 33 male mice (12.7±0.5 weeks, 14 anxA7$^{+/+}$, 19 anxA7$^{-/-}$) were examined in inhalative anaesthesia by transvenous intracardiac atrial and ventricular stimulation. Baseline ECG- and electrophysiologic parameters as well as incidence and inducibility of atrial and ventricular arrhythmias were evaluated.
Results: The surface ECG of anxA7$^{-/-}$ showed a significantly shorter P-wave (14.9±3.7ms vs. 18.1±2.7ms; $P<0.01$) and QRS-interval (15.3±2.4ms vs. 17.4±2.7ms, $P<0.05$) as compared to anxA7$^{+/+}$. AnxA7$^{-/-}$ showed significant higher susceptibility to induction of atrial fibrillation (AF) (4.4±1.7 vs. 2.7±2.0 inducible episodes/animal; $p<0.02$). As major finding, sustained AF >30min was found in 4 of 19 anxA7$^{-/-}$, whereas the longest episode in anxA7$^{+/+}$ lasted only 480.1sec. Incidence of ventricular tachycardia (VT) was significantly higher in anxA7$^{-/-}$ after programmed (3.8±3.1 vs. 0.6±1.1 inducible episodes/animal; $P<0.01$) and burst ventricular stimulation (2.6±3.2 vs. 0.7±1.1 episodes/animal; $P<0.05$); VT lasted significantly longer in mutant mice. These findings were accompanied by the presence of relevant Ca^{2+}-overload in anxA7$^{-/-}$ ventricular tissue.
Conclusions: AnxA7-deficiency significantly elevates susceptibility to atrial and ventricular arrhythmia and perpetuates AF in a relevant part of the investigated animals. These observations might be attributable to alterations of Ca^{2+}-homeostasis and Ca^{2+}-overload in murine cardiomyocytes.

1163-260 Enalapril Preserves Sinus Node Function in a Canine Atrial Fibrillation Model Induced by Rapid Atrial Pacing

Masao Sakabe, Akira Fujiki, Hidehiko Nagasawa, Kunihiro Nishida, Masataka Sugao, Takayuki Tsuneda, Hiroshi Inoue, Toyama Medical and Pharmaceutical University, Toyama, Japan

Effects of enalapril on canine sinus node (SN) dysfunction induced by rapid atrial pacing were investigated.
Methods: Seventeen beagles were pretreated with placebo (G-I, n=9) or enalapril 1mg/kg/day (G-II, n=8). All beagles were paced at 500bpm from the right atrial appendage for 4 weeks. Six sham dogs were serving as the control for histological analyses.
After 30 sec overdrive pacing, the longest interval from the last paced atrial depolarization to the first spontaneous sinus cycle was recorded as sinus node recovery time (SNRT). SNRT, intrinsic SN cycle length (SCL), atrial effective refractory period (AERP) and the duration of AF were measured every week. Corrected SNRT (CSNRT) was defined as SNRT minus SCL.
After 4 weeks pacing, quantitative analysis of interstitial fibrosis (IF) and fatty degeneration in SN was performed with Masson's trichrome stain, and apoptosis of sinus nodal cell was detected with TUNEL method.
Results: In G-I, rapid atrial pacing progressively prolonged CSNRT (from 260.0 ± 25.8 to 717.4 ± 51.5 ms:$p<0.005$). In G-II enalapril shortened CSNRT (409.8 ± 37.2ms: $p<0.005$) compared with in G-I after 4weeks of pacing. SCL was shorter in G-II than in G-I after 4weeks of pacing (426 ± 33.7 v.s. 567.6 ± 72.6ms:$p<0.05$). AERP did not differ between two groups. The duration of AF was significantly shorter in G-II (3.6 ± 0.7sec) than in G-I (48.3 ± 10.5sec: $p<0.005$).
In the SN area IF in G-I (9.7 ± 1.9%: $p<0.05$) was greater than in sham group (2.4 ± 0.9%). Enalapril significantly suppressed the fibrosis in G-II (4.0 ± 2.0%: $p<0.05$). Infiltration of fat into the SN was significantly greater in G-I (32.6 ± 5.9%) compared with sham group (4.2 ± 2.1%: $p<0.005$) and G-II (4.0 ± 1.7%: $p<0.005$). In regard to atrium, IF was also significantly greater in G-I (13.3 ± 5.1%) compared with sham group (1.4 ± 0.5%: $p<0.05$) and G-II (1.5 ± 0.4%: $p<0.05$). TUNNEL positive cells were observed in three of nine dogs in Group-I, but none in sham and Group-II.
Conclusions: Rapid atrial pacing impaired sinus node function with fibrosis and fatty degeneration of sinus nodal cells and enalapril prevented the change. These findings suggest the suppression of degenerative changes in SN by enalapril may preserve sinus node function in AF.

1163-261 Three Dimensional Mapping of Postshock Activation After Ventricular Defibrillation in Pig Hearts

Xianhong Fang, Gregory P. Walcott, Cheryl R. Killingsworth, Dennis Rollins, Anthony L. Sims, William Smith, Raymond E. Ideker, University of Alabama at Birmingham, Birmingham, AL

Background: The exact mechanism of defibrillation is still controversial. One debated issue is the spread pattern of postshock activation. Reentrant and focal activation patterns both have been observed in previous studies with a shock strength near the defibrillation

threshold (DFT). Since mapping in most of these studies was confined to the epicardium, we evaluated postshock activation after defibrillation in 3 dimensions in vivo in pig hearts using plunge needles.
Methods: In 6 open-chest pigs, 84 plunge needles each containing 6 (LV) or 4 (RV) electrodes 2 mm apart were inserted throughout both ventricular free walls. After inducing ventricular fibrillation, shocks of DFT strength and of sub-DFT strength (20% below DFT voltage) were given from defibrillation electrodes in the RV and SVC. After the study, the distances between electrodes were determined by manual digitization of the plunge needle locations.
Results: In 28 of the 43 (65%) defibrillation episodes, the site of earliest postshock activation was recorded in the subepicardial electrodes within 4 mm of the epicardium near the LV apex. A total of 141 double potentials (DPs) were recorded near the earliest postshock activation site, 68 (48%) of which were in the subepicardium. In 31 of the 43 defibrillation episodes, a complete intramural reentrant circuit was observed near the LV apex. The perimeter of this reentrant circuit was significantly larger following sub-DFT shocks than following DFT strength shocks (55±10 versus 46±9 mm, p<0.01).
Conclusion: This 3 dimensional mapping study revealed intramural reentry during the first postshock activation cycle in most failed defibrillation episodes. As the shock strength increased nearer to the DFT, the size of the reentrant pathway decreased. Approximately two-thirds of the earliest postshock activation sites and and half of DPs were located in the subepicardium, the most distal extent of the Purkinje fiber distribution in pig hearts.

1163-262 Decreased Arrhythmia Vulnerability in a Novel Rabbit Model of Left Ventricular Aneurysm Repair

Hirotsugu Yamada, Yoshio Ootaki, Zoran Popovic, Masao Daimon, Keiji Kamohara, Don Wallick, James Thomas, David Van Wagoner, Kiyotaka Fukamachi, Yuanna Cheng, The Cleveland Clinic Foundation, Cleveland, OH

Background: Left ventricular (LV) aneurysm repair is a surgical technique that aims to restore cardiac geometry and function. The electrophysiologic impact of such surgical intervention is less known.
Methods: Myocardial infarction (MI) was created by ligation of proximal left circumflex artery in 4 rabbits, resulting in LV apical aneurysm. After 4 weeks, rabbits underwent LV repair by plication of the akinetic LV region using epicardial and transesophageal echocardiography (echo) via intracardiac ultrasound catheter. LV end-diastolic (EDV) and end-systolic (ESV) volumes were measured by transthoracic echo before and weekly after LV repair. Fast fluorescence imaging with voltage-sensitive dyes was performed on Langendorff-perfused rabbit hearts 4 weeks post-plication. Shock-induced vulnerability was assessed using monophasic shocks of ±100V, ±130V, ±160V, ±190V and ±220V applied at 25%, 50% and 75% of action potential duration (APD), delivered via a right ventricular lead from a 150μF capacitor defibrillator. Vulnerability data were compared with data from structurally normal (n=8) and healed-infarct hearts (4 weeks or older, n=8) by grouping anodal or cathodal shocks applied at all phases of APD.
Results: LV repair reduced EDV (4.7±1.0 to 3.5±0.6 ml, p<0.05) and ESV (2.6±0.6 to 1.5±0.2 ml, p<0.01) and increased LV ejection fraction (EF) (44.6±6.8 to 56.7±5.8 %, p<0.01). EF was 54.8±6.2% at 1 week and 52.0±1.8% at 3 weeks after plication. Incidence of shock-induced sustained arrhythmia (6 or more post-shock extra beats) post-plication was comparable to normal hearts but substantially reduced compared to infarcted, nonplicated hearts (anodal shocks: 6.7% vs. 33%, p<0.001; cathodal shocks: 33% vs. 70%, p<0.001). There was also striking reduction in the incidence of long lasting arrhythmia (>30 sec, required rescue shock to terminate) in plicated vs. infarcted hearts (anodal shocks: 0% vs. 30%, p<0.001; cathodal shocks: 6.7% vs. 59%, p<0.001).
Conclusion: This study demonstrates that hemodynamic improvement following infarct plication is accompanied by a striking reduction of arrhythmia vulnerability and incidence, suggesting a potential benefit of this therapeutic approach.

POSTER SESSION

1164 Ablation and Surgery for Atrial Fibrillation

Tuesday, March 08, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 3:30 p.m.-4:30 p.m.

1164-247 Significance Of A Thermal Effect On Vagal Nerve System During Ablation In Pulmonary Veins; Analysis Using Our Thermal Balloon Catheter

Kazushi Tanaka, Hiroshi Sohara, Shuutaro Satake, Shigeru Saitou, Yoshio Watanabe, Shonan Kamakura General Hospital, Kamakura-shi, Japan

We retrospectively evaluated an effect of vagal modification (VM) induced by pulmonary vein (PV) isolation on the recurrence of paroxysmal atrial fibrillation (PAF).
Methods: The study population consisted of 21 patients with PAF treated by radiofrequency catheter ablation (RFA) using our original thermal balloon catheter. Exclusion criteria were as follows; sick sinus syndrome, injection of atropine sulfate during the procedure, frequent appearance of atrial premature beats or taking a beta-blocker. The initial RFA targeting the left superior PV was commenced at 55°C of the balloon surface temperature with energy delivery duration for 3-5 minutes. Unless the elimination of all the PV potentials could be obtained, the procedure was repeated in a step-up of the temperature by 2-3°C. Subsequently, the same protocol was applied to the right superior PV, and if possible, next the left inferior PV and finally the right inferior PV. To evaluate the vagal activity, all the sinus cycle lengths (SCLs) during the energy delivery were measured. The fluctuation exceeding 100ms of the SCLs was conveniently determined as the VM; namely, the prolongation of the SCLs as the vagal reflex and the shortening of the SCLs following the reflex as the vagal denervation.
Results: Mean attempts of the energy delivery for the left superior PVs, right superior PVs, left inferior PVs and right inferior PVs were 2.8, 1.7, 1.8 and 1.5, respectively. After all, the vagal reflex and/or denervation were observed in 10 patients (the group VM+, a mean age of 56 ± 11 years), and the remaining 11 patients were assigned to the group VM- (56 ± 11 years). In the group VM+, the VM was observed during the RFAs of the left superior PVs in all patients, in one of whom it also appeared during the left inferior PV. However, this phenomenon could not be induced during the RFAs of the right PVs. In a mean follow-up period of 24 ± 5 (17-30) months, the recurrence of PAF was observed in 10% of the group VM+ vs. in 45% of the group VM- (P=0.0127 by log-rank test).
Conclusions: These results may indicate that the vagal innervation near the PVs is inhomogeneous and has a trend to converge around the left superior PV and that the VM can reduce the recurrence rate of PAF in a chronic period.

1164-248 Changes in Left Atrial Size and Function by Magnetic Resonance Imaging After Left Atrial Linear Ablation

Thomas M. Meyer, Robert L. Eisner, David B. Delurgio, Fernando V. Mera, Angel R. Leon, Emory Crawford Long Hospital, Atlanta, GA

Background: Left atrial (LA) linear radiofrequency (RF) ablation has been shown to be effective in the elimination of atrial fibrillation (AF). Whether the extensive LA lesions involved in this procedure affect atrial function and geometry has not been thoroughly studied. Therefore, we sought to determine the effects of LA linear ablation on atrial remodeling by measuring changes in LA volume and ejection fraction (EF).
Methods: Eleven patients with AF underwent LA ablation. Contrast-enhanced magnetic resonance angiography (CE-MRA) and cine magnetic resonance (MR) of the left atrium were performed before and 3 months after ablation. LA volume was measured from the CE-MRA. In addition, for six patients that were in sinus rhythm during both the pre and post MR, an atrial ejection fraction (EF) was measured by cine magnetic resonance (MR).
Results: Changes in LA volume and EF before and after ablation for individual patients and as a mean are reported in the Table. Most patients (except Patients 2 & 4) had a significant decrease in LA volume after ablation. In the six patients in whom EF could be calculated, all but Patient 1 had a decrease in LA EF.
Conclusions: In most patients, LA linear RF ablation results in a reduction in LA volumes. However, this apparent positive remodeling does not translate into improved atrial function as measured by LA EF. In fact, atrial function may actually worsen after extensive LA ablation.

Table

Patient	LA Volume,ml (pre)	LA Volume,ml (post)	Volume Change (%)	LA EF % (pre)	LA EF % (post)	EF Change %
1	116	101	-13%	40	43	+8
2	72	95	+32%	54	40	-26
3	99	76	-23%	48	34	-29
4	83	104	+25%	46	35	-24
5	94	92	-2%	45	40	-11
6	92	63	-32%	46	37	-20
7	71	53	-25%	N/A	N/A	
8	115	89	-23%	N/A	N/A	
9	72	67	-7%	N/A	N/A	
10	81	73	-10%	N/A	N/A	
11	136	124	-9%	N/A	N/A	
MEAN	94 (+/-21)	85 (+/-21)	-8% (+/-20) (p=0.13)	52 (+/-14)	38 (+/-3)	-17%(+/-14) (p=0.10)

1164-249 A Combined Approach in the Catheter Ablation of Atrial Fibrillation: Circumferential Left Atrial Ablation With Electrical Isolation of the Pulmonary Veins

Jesse S. Sethi, Bryan Piedad, John R. Bullinga, David Feigenblum, Jason Chinitz, Douglas Holmes, Neil Bernstein, Larry Chinitz, NYU Medical Center, New York, NY

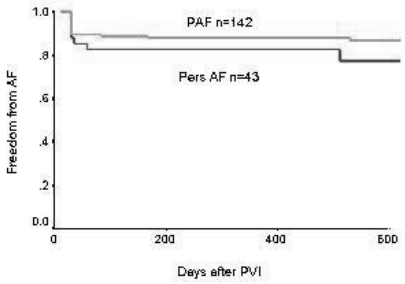
Background- Circumferential left atrial catheter ablation (LACA) and segmental ostial catheter ablation (SOCA) of the pulmonary veins (PV) have both been shown to be efficacious techniques in the treatment of atrial fibrillation (AF). However, there is conflicting data as to which approach confers better clinical outcomes. We employed a combined approach, performing LACA followed by SOCA to ensure PV isolation. There is no prior data reported on such an approach.
Methods- 154 consecutive patients (mean age 55 ± 11 yrs, 119 males) with paroxysmal (133 pts) or persistent (21 pts) AF underwent either SOCA (91 pts) or a combined approach (LACA+SOCA - 63 pts). SOCA was performed using an 8-mm tip ablation catheter and a 10-pole circular mapping catheter. LACA+SOCA utilized an 8-mm tip ablation catheter and the assistance of a non-fluoroscopic, three-dimensional, surface electrode-based navigation system (NavX, Endocardial Solutions). After LACA, the circular mapping catheter was positioned at the ostia of each of the PVs, and SOCA was performed.
Results- The mean procedure time was 165 ± 50 min in the SOCA group and 179 ± 59 min in the LACA+SOCA group (p=NS). After completion of LACA, there was incomplete electrical isolation in a mean of 2.61 ± 0.78 PVs per patient. Subsequent SOCA required a mean of 18.1 ± 7 additional ablation lesions per patient (mean of 10 ± 4.5 min of ablation time) to achieve complete electrical isolation of the PVs. At a mean follow-up of 13.9 ± 9.3 months, the incidence of AF recurrence was 32.9% in the patients who underwent SOCA and 17.5% in the patients who underwent LACA+SOCA (p=0.03). Among the variables of male sex, age, presence of persistent AF, hypertension, diabetes, enlarged left atrium or reduced left ventricular ejection fraction, only the utilization of the SOCA technique as

opposed to SOCA+LACA was an independent predictor of AF recurrence. There were two adverse events in the SOCA group (stroke, tamponade) and one (tamponade) in the LACA+SOCA group (p=NS).
Conclusions- A combined approach of LACA followed by SOCA significantly reduces AF recurrence compared with SOCA alone, and ensures an electrical endpoint without a significant increase in complications or procedure time.

1164-250 Pulmonary Vein Isolation Yields High Success Rates in Persistent Atrial Fibrillation

Tina C. Sichrovsky, Aysha Arshad, Sandeep Joshi, Amit Kamra, Lance Weathers, Jonathan S. Steinberg, St.Luke's-Roosevelt Hospital Center, New York, NY

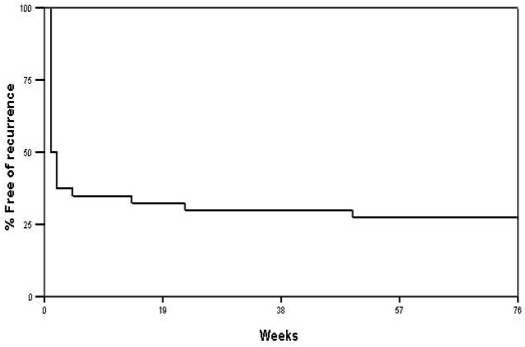
Background: Pulmonary vein isolation (PVI) for the treatment of paroxysmal atrial fibrillation (PAF) has excellent success rates. Since published outcomes for persistent (pers) AF are low (<25%), many centers use alternative approaches. The lower success rate may be due to pronounced, but potentially reversible, remodeling. We compared our PVI experience in persAF, when pretreated with cardioversion and antiarrhythmic drugs (AAD), to PAF.
Methods and Results: 185 consecutive patients (pts), (age 56±11 years, 73% male) underwent PVI, 142 (76%) had PAF and 43 (24%) persAF. There was no difference in age, underlying cardiovascular disease, left ventricular function or left atrial enlargement between groups. Pts with persAF had a shorter total history of AF (1.0±0.8 vs 6.3 ±6.5 years, p< 0.001) than pts with PAF.
Pts with persAF received dofetilide (40%), amiodarone (19%) or sotalol (12%) for 1 month pre- and post-PVI and 66% were in sinus rhythm (SR) at PVI. AADs were discontinued at 1 month, and during follow-up of 585±351 days, freedom from recurrence off AADs was achieved in 81% of pts with persAF compared to 87% of pts with PAF (p=NS). Marked improvement with decreased AF burden was achieved in 85% of pts with persAF and 95% of pts with PAF (p=NS)
Conclusions: Pts with persAF have outcomes after PVI comparable to pts with PAF, perhaps related to peri-procedure reverse remodeling facilitated by return to SR with cardioversion and short-term AAD treatment. These pts should be considered acceptable candidates for PVI.



1164-251 Time Interval From Pulmonary Vein Isolation Using Cryoablation to the First Atrial Fibrillation Recurrence

Yves Van Belle, Carl Timmermans, Randy Manusama, Maud Van De Schoot, Suzanne Philippens, Harry Crijns, Luz-Maria Rodriguez, Academic Hospital Maastricht, Maastricht, The Netherlands

BACKGROUND: This study was designed to observe the time interval from pulmonary vein isolation (PVI) to the first recurrence of atrial fibrillation.
METHODS: Forty patients (31 men; age 47±10 years) underwent segmental PVI with cryoablation (single session: n=37, double session: n=3). All patients had drug resistant PAF (2.0±1.3 failed AAD's) without structural heart disease (LA diameter 40±5 mm, LVEF 59±9%, AF duration 4±3 years). Transtelephonic Holter monitoring was used on a daily and symptomatic basis during 1 month before PVI and 3 to 6 months after, followed by visits to our outpatient clinic every 2 months. Patients were all highly symptomatic and kept a diary of AF related symptoms during that same period.
RESULTS: A mean of 2.5±0.7 PV's per patient were ablated. AF recurrence was observed in 30 out of 40 patients (75%). The mean time to first recurrence was 17.5 days (range 1-165). The majority of recurrences (83%) occurred within 14 days after PVI (figure). After a follow up of 490±351 days 63% of patients (25/40) were free of AF.
CONCLUSIONS: Long term follow-up shows that the first AF recurrence after cryoablation for pulmonary vein isolation occurs frequently and especially early after the procedure. Although a large number of patients have short term recurrence, the majority of them (63%) become free of AF after more than a year.



1164-252 Does Increased Area of Pulmonary Vein Isolation Decrease the Number of Non Pulmonary Initiators of Atrial Fibrillation?

Ron D b Simon, Scott Burke, Lacy Sturdivant, Robert Leman, Michael R. Gold, Barbara Knick, J Marcus Wharton, MUSC, Charleston, SC

Background: Atrial fibrillation (AF) ablation should probably involve pulmonary vein (PV) isolation and ablation of non-pulmonary initiators (NPIs). The optimal method for achieving this remains controversial. Three possible approaches are: Method 1: an ostial segmental PV isolation; Method 2: a periostial anatomical PV isolation; and Method 3: a wide area circumferential ablation (WACA) including a roof and left atrial isthmus line guided by electroanatomical mapping. Theoretically, the number of NPI sites in the left atrium will be reduced by Method 2 and more so by Method 3, compared with Method 1, making the subsequent ablation of NPIs less arduous and possibly unnecessary.
Methods: We performed AF ablation on 171 consecutive patients using Methods 1, 2, and 3 in consecutive cohorts. NPIs were then mapped and ablated. NPIs caused either repetitive premature atrial complexes, atrial tachycardia and/or AF, either spontaneously or after atrial burst pacing or induction of AF followed by DC cardioversion, on or off isoproterenol. The percentage of patients with NPIs in each ablation group seen after PV isolation was analyzed.
Results: AF ablations were performed in 171 patients, with groups equivalently matched for age, gender, and presence of cardiovascular disease. The percentage of patients with NPIs with Methods 1, 2, and 3 was similar (49%, 53%, and 55%, respectively). The percentage of right sided NPIs in each group were 23%, 44%, and 35%. The percentage of left sided NPIs were 38%, 35% and 26%. The percentage of patients free of AF at 5 months was 75%, 75% and 95%, respectively, for Methods 1, 2, and 3.
Conclusions: The total number of NPIs is high and unaffected by the ablation method. WACA does not reduce the number of NPIs and additional ablation of NPIs with WACA may increase the single procedure success rate.

1164-267 Mechanisms And Management Of Left Atrial Tachycardia Following Circumferential Left Atrial Ablation For Atrial Fibrillation

Carlo Pappone, Giuseppe Augello, Francesco Manguso, Nicoleta Sora, Valter Tortoriello, Gabriele Vicedomini, Vincenzo Santinelli, San Raffaele University Hospital, Milan, Italy

Background - We demonstrated that a modified circumferential PV ablation (CPVA-M) approach including additional lines on posterior wall and the mitral isthmus, reduces the incidence of left atrial tachycardia (LAT) after ablation.
Methods - A total of 420 patients underwent CPVA-M and were followed for 1 year. The endpoint was freedom from LAT after CPVA-M. There was a six-week blanking period during which arrhythmia occurrence was regarded as a transient phenomenon.
Results - Overall, 54 (13%) patients had recurrent AF beyond the blanking period. During the six-week blanking period, 38 (9%) patients had episodes of LAT. Beyond this blanking period, AT spontaneously resolved in 21 (56%, p = 0.01) patients. As a result, 17 of 420 (4%, including 2 with AF recurrence) continued to experience AT. The mean time interval between the initial procedure and the first occurrence of AT was 2.8±0.7 months. AT was incessant in all patients and in 12 of them resulted in syncope. Patients with incessant AT underwent a repeat procedure 4.8±0.6 months after the index procedure. Only multiple gaps were found in the 73% at the second procedure, whereas at the end of the first procedure single gaps were present in 9%, and multiple in 64%, suggesting that recovery of conduction was an important factor in the occurrence of AT. Among patients with macroreentrant AT, the critical isthmus was localized to the area between the mitral annulus and the left inferior PVin 4 after CPVA-M, the area between the right PVs (4) or between the left PVs (4) with the circuit passing between the two ipsilateral veins at the site where previous intervenous lines were performed. In less than one third of patients AT was focal. RF ablation was successful in eliminating AT in all patients with up to 5 RF applications delivered on the earliest site for focal AT and on the critical isthmus for macroreentrant AT.
Conclusions. Incessant AT after CPVA is a relatively common complication and its persistence often can result in syncope. Incessant AT requires a repeat procedure. However, postablation AT may be a transient phenomenon in more than a half of cases.

1164-268 Successful Outcome with Targeted Ablation Strategy for Atrial Fibrillation: Patient Characteristics

William H. Sauer, Stuart Jay Beldner, Melissa L. McKernan, David Lin, Sanjay Dixit, Edward P. Gerstenfeld, David J. Callans, Francis E. Marchlinski, University of Pennsylvania, Philadelphia, PA

Background: An anatomic approach with empiric isolation of all pulmonary veins (PVs) for ablation of atrial fibrillation (AF) has been advocated. However, some patients may benefit from a more selective approach targeting AF triggers, thereby minimizing the potential for ablation related complications. We attempted to identify the clinical characteristics of such patients.
Methods: Data on 278 patients undergoing AF ablation between November 2000 and May 2003 was retrospectively analyzed to assess for potential clinical characteristics associated with fewer AF triggers. Electrophysiological studies using multipolar catheters in both atria during isoproterenol infusion (titrated up to 20 mcg/min) identified triggers initiating AF as originating from a pulmonary vein or other atrial source. Atrial fibrillation control was defined as no atrial fibrillation on or off an anti-arrhythmic drug, or marked (>90%) reduction in symptoms. Follow up data included trans-telephonic monitoring and clinical data collection from patient interviews. The clinical characteristics of patients with successful ablation targeting 3 PV isolations.
Results: The average follow up for patients with AF control was 21.2 +/- 9.1 months (range 6 to 47 months). AF control was achieved in 190 of the 213 patients (89%) with more than 2 veins isolated and 57 of the 65 patients (88%) with fewer triggers of AF ablated. Of these 57 patients, 11 patients had 1 PV, 42 patients had 2 PVs, and 5 patients had non-PV triggers targeted. There were no significant differences between the two groups of patients with respect to gender, duration of AF symptoms, left atrial size, or presence of mitral regurgitation or LV dysfunction. Successful ablation of AF triggers in 2 veins or fewer was associated with younger age (51 vs. 56 years; P=0.01), absence of hypertension (27.3% vs. 47.3%; P=0.01), and a history of paroxysmal AF (93.7 % vs 73.2%; P<0.01).
Conclusion: Absence of hypertension, younger age, and history of paroxysmal AF are associated with the presence of fewer arrhythmogenic pulmonary veins. Therefore, empiric isolation of all pulmonary veins in this group of patients may be unnecessary.

1164-269 The Need For Atrial Flutter Ablation Following Pulmonary Vein Antrum Isolation in Patients With And Without Prior Cardiac Surgery

Fethi Kilicaslan, Hirosuke Yamaji, Atul Verma, Nassir F Marrouche, Oussama Wazni, Jennifer E Cummings, Steven Hao, Michael Williams Andrews, Salwa Beheiry, William A Belden, Stephan Minor, George Joseph, David O Martin, J David Burkhardt, Walid Saliba, Robert A Schweikert, Andrea Natale, The Cleveland Clinic Foundation, Cleveland, OH, Sutter Pasific Heart Centers, San Francisco, CA

Background: Atrial fibrillation (AF) and atrial flutter (AFL) often coexist. Pulmonary vein (PV) triggers may induce both arrhythmias and pulmonary vein antrum isolation (PVAI) may be sufficient to control both. However, in patients with prior cardiac surgery (PCS), atrial incisions and scar areas may cause AFL recurrence despite elimination of PV triggers.
Objectives: To assess the incidence of AFL after PVAI in patients with PCS in comparison to patients without PCS and to assess the need for AFL ablation in both groups.
Methods: Data from 1125 patients who had PVAI between 10/2000 and 12/2003 were analyzed. Of them, 63 patients (Group 1, 12 female, mean age 57±13 years) had PCS > 6 months ago and the remaining 1062 had no history of PCS (Group 2, 212 female, mean age 55±12 years). Patients who had AFL ablation before or during PVAI were excluded from analysis. Patients with and without PCS did not differ in their age, duration and type of AF. Patients in Group 1 had larger left atrial diameter (4.7±0.7 vs 4.4±0.6, p=0.0001), higher incidence of AFL pre-PVAI (38% vs 22%, p=0.005), and lower ejection fraction (49±10 vs 54±8, p=0.0001).
Results: There was no significant difference in post-PVAI AF recurrence between Groups 1 and 2 (21% vs. 19% respectively, p=0.74). But AFL incidence post-PVAI was significantly higher in Group 1. 21 patients (33%) in Group 1 had AFL (7 typical, 14 atypical) compared to 43 patients (4%) in Group 2 (28 typical, 15 atypical). Ablation of the AFL in Group 1 patients resulted in an 81% acute success rate with 12% recurrence over a mean follow-up of 357±201 days.
Conclusions: In patients with PCS, post-PVAI AF recurrence is similar to patients without PCS. However, history of PCS is associated with a higher recurrence of AFL after PVAI. In a significant number of patients with PCS, AFL ablation is required to achieve cure.

1164-270 Cost-Effectiveness of Left Atrial Catheter Ablation, Anti-Arrhythmic Therapy, and Rate Control for Paroxysmal and Chronic Atrial Fibrillation

Paul Chan, Sandeep Vijan, Fred Morady, Hakan Oral, University of Michigan, Ann Arbor, MI

Background: Left atrial catheter ablation (LACA) has been performed for paroxysmal and chronic atrial fibrillation (AF). However there is limited data on cost-effectiveness of LACA for AF.
Objectives: To compare the cost-effectiveness of LACA, rhythm control with amiodarone, and rate control in patients with paroxysmal (PAF) and chronic AF (CAF) at low and moderate risk for stroke.
Methods: Based on published data and hospital accounting information, cost-effectiveness of 3 therapeutic strategies of LACA, anti-arrhythmic therapy with amiodarone, and rate control with antithrombotic therapy (aspirin or warfarin for low risk, and warfarin for moderate risk) were assessed in 2 hypothetical cohorts of 55 year-old patients with PAF at low risk for stroke, and 65 year-old patients with PAF and CAF at low and moderate risks for stroke using a Markov model. Outcomes of expected cost, quality-adjusted life years (QALYs), and incremental cost-effectiveness were determined for patient life-time, at 6-month cycles.
Results: For 65 year-old AF patients at low risk for stroke (1.4%/year), each treatment strategy when paired with aspirin dominated therapy with warfarin. LACA with aspirin was the most cost-effective ($51,387/QALY for PAF and $61,700/QALY for CAF). LACA with aspirin therapy also was more cost-effective for 55 year-old patients with PAF ($27,697/QALY). For AF patients with moderate stroke risk (3.0%/year), LACA with warfarin therapy was the most cost-effective ($18,742/QALY for PAF and $21,629/QALY for CAF). Sensitivity analyses demonstrated that the choice of optimal strategy and cost-effectiveness was primarily influenced by the baseline stroke risk, rate of stroke in sinus rhythm, efficacy of coumadin and aspirin therapy in preventing stroke, efficacy of the three therapies, and cost of LACA.
Conclusion: LACA is cost-effective in patients with PAF and CAF who are at moderate risk for stroke. Among patients who are at low risk for stroke, LACA is cost-effective in the 55 year-old cohort with PAF, whereas for the 65 year-old cohort with PAF or CAF, decisions for LACA therapy depend largely on patient preferences, efficacy of the procedure, and society's willingness to pay for such therapy.

1164-271 Minimally Invasive Bilateral Epicardial Pulmonary Vein Isolation And Left Atrial Appendage Exclusion

Eric W. Schneeberger, Randall K. Wolf, John B. Flege, Jr., Walter H. Merrill, University of Cincinnati College of Medicine, Cincinnati, OH

BACKGROUND. The Cox Maze procedure, was seldom performed because of its complexity and invasiveness despite it's effectiveness. Pulmonary vein isolation has been shown to be curative in a number of patients with AF. Catheter techniques have demonstrated mixed results due to the variations in endocardial topography and the propensity for delivery of non-transmural lesions. A number of complications have also been reported. A new approach that results in electrical isolation of the pulmonary veins has been achieved at surgery by placing a bi-polar radio frequency device on the atrium just medial to the pulmonary veins (on the atrial cuff).
METHODS. Twenty-five patients (4 female) (20 paroxysmal, 3 persistent, 2 permanent with signed consent who agreed to 6 months of follow up) were treated using a minimally invasive bilateral surgical procedure. The indications for operation were: symptomatic AF despite maximal drug therapy, antiarrhythmic drug side effects, intolerance to warfarin and history of TIA or stroke. After encircling the veins, a bi-polar clamp was passed through a port site and around both sets of pulmonary veins. Isolation of the atrial cuff was achieved in less than 15 seconds. The left atrial appendage was removed by a stapling device fed through a port site with TEE control.
RESULTS. 25 symptomatic AF were treated and there were no perioperative complications or blood product usage. The average time for the procedure was: 186mins (Rt Side 83 mins, Turning16mins, Lt Side 87 mins). Pain was graded by the patients as: 3.5/10 at 24 hours. All patients left hospital on their preoperative medications and were weaned from them at follow up visits. To date all patients are in sinus rhythm (by 1 week monitoring) and are asymptomatic with an average follow up of 124 days.
CONCLUSIONS. Minimally invasive bilateral epicardial pulmonary vein isolation (in which encircling transmural atrial lesions are created and in which the left atrial appendage is excluded) may have a role as a stand alone procedure to cure atrial fibrillation. A clinical trial is being designed to confirm its efficacy. Longer term follow up is warranted.

1164-272 Inferior Right Atrial Wall as a Predilection Site of Atrial Arrhythmias in Patients with Tricuspid Atresia.

Natasja M. de Groot, Wing King Chan, Nico Blom, Ernst E. van der Wall, Martin J. Schalij, Leiden University Medical Center, Leiden, The Netherlands

Atrial tachycardias (AT) frequently occur in patients with tricuspid atresia (TA) late after corrective or palliative cardiac surgery. Mapping prior to ablation has proven to be mandatory for identification of crucial pathways of conduction during ART and to select the most optimal ablation strategy. In this study, we analysed the relation between the location of crucial pathways of conduction and spatial distribution of right atrial bipolar voltages.
Method: Patients (n=12, 28±12 yrs, 5 male) with TA and AT were studied. 3D electro-anatomical bipolar mapping was performed during AT. Ablation was targeted at crucial pathways of conduction. Spatial distribution of peak-to-peak voltages of bipolar electrograms were off-line analysed in antero-posterior (A-P) and postero-anterior (P-A) view of the reconstructed right atrium. The X, Y and Z-axis were in both views used to subdivide the right atrium in a high lateral (HL), low lateral (LL), high septal (HS) and low septal quadrant (LS).
Results: Eighteen different AT's (CL 309±76 ms) were mapped and ablated. The underlying mechanism was reentry (n=17) or a focus (n=1). Crucial pathways of conduction were located in the P-A view between 1) areas of scar tissue (n=17) and 2) the inferior caval vein and scar tissue in the lower lateral area (n=1). Bipolar voltages of these quadrants were significant lower than in the remainder of the atria (table).
Conclusion: In TA patients, most post-operative AT originate from low voltage areas in the inferior right atrial wall.

	N	median V (mV)	P_5	P_{95}
AP-HL	434	0,56	0,06	3,56
AP-LL	513	0,58	0,06	4,33
AP-HS	448	1,1	0,07	4,73
AP-LS	363	0,43	0,07	4,77
PA-HL	349	0,46	0,05	5,05
PA-LL	340	0,21*	0,04	1,83
PA-HS	407	0,30	0,04	1,90
PA-LS	575	0,17*	0,03	1,51

*p<0,01

ORAL CONTRIBUTIONS

882FO Featured Oral Session...Noninvasive Markers of Arrhythmia Vulnerability

Wednesday, March 09, 2005, 10:30 a.m.-Noon
Orange County Convention Center, Room 231A

10:45 a.m.

882-4 A New Technique for the Quantitative Assessment of Repolarization Variability in Holter ECGs: Evaluation on the ICD Population of Madit II

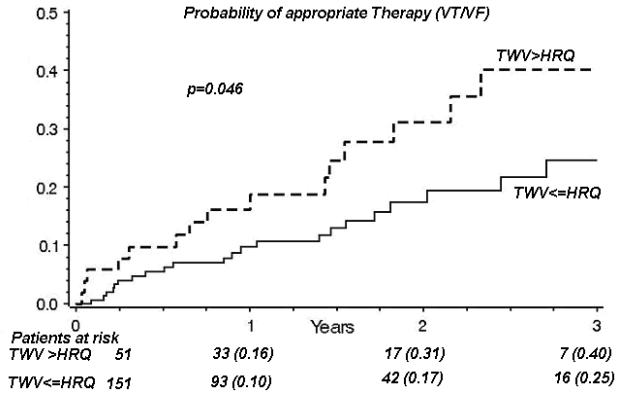
Jean-Philippe Y. Couderc, Wojciech Zareba, Scott McNitt, Arthur J. Moss, University of Rochester Medical Center, Rochester, NY

T-wave variability (TWV) is associated with electrical instability of the myocardium leading to malignant arrhythmias and sudden cardiac death. In this study, we present a novel approach for the measurement of T-wave variability. We investigated the prognostic significance of TWV in patients (pts) from the Multicenter Automatic Defibrillator Implantation Trial II (MADIT II) population with and without appropriate ICD therapy (AIT).

Method: the exclusion criteria of pts in the ICD arm were: abnormal conduction, right or left bundle branch block or QRS duration >120 ms. TWV was measured based on amplitude variance of T-wave amplitude.

Results: a group of 202 pts were analyzed, 39 pts had AIT. No significant differences were found between the 2 groups for age, QRS duration, BUN, gender and BMI. After adjustment for heart rate, ejection fraction, a Cox proportional-hazards regression model revealed that TWV values were predictive for AIT (HR: 3.3, CI:1.3-7.6, p=0.0049). Based on the higher quartile values (HRQ) of TWV in the no AIT group, an increased TWV value was associated with a significant increased probability of AIT (see figure, p=0.046).

Conclusion: we designed a method for the assessment of repolarization instability in ambulatory Holter recordings. The method is able to detect transient variability of T-wave amplitude. In the ICD arm of the MADIT II population, the method revealed an increased variability of repolarization predicting the occurrence of VT/VF events (documented by ICD interrogation).



11:00 a.m.

882-5 Heart Rate Turbulence: An Useful Non Invasive Risk Predictor In Patients With Myotonic Dystrophy Type 1.

Michela Casella, Antonio Dello Russo, Loredana Messano, Sergio Valsecchi, Alfonso Sestito, Gemma Pelargonio, Giuseppe De Martino, Manuela Pace, Tommaso Sanna, Maria Lucia Narducci, Gianluigi Bencardino, Fortunato Mangiola, Gaetano Antonio Lanza, Paolo Zecchi, Fulvio Bellocci, Cardiovascular Department Catholic University, Rome, Italy, Centre for Neuromuscular Diseases, Rome, Italy

Background. Myotonic Dystrophy type 1 (DM1) is a multisystemic disorder with cardiac complications and life-threatening arrhythmias. Heart rate turbulence (HRT) is a noninvasive tool for risk stratification. Aim of our study is to assess HRT in DM1 patients in comparison to patients with frequent ventricular arrhythmias and structurally normal heart (VANH). We also evaluated the correlation between HRT and sustained ventricular arrhythmias induced at electrophysiological study in DM1 patients.

Methods. We performed HRT analysis, by 24 hours Holter recording, in 15 DM1 (mean age 52±10 yrs) and in 15 VANH patients (mean age 54±9 yrs). We calculated: turbulence onset (TO), a percentage difference between the mean of first 2 RR intervals after and the last 2 RR intervals before a premature ventricular contraction, and turbulence slope (TS), a maximum positive slope of a regression line assessed over any 5 consecutive RR intervals within the first 20 RR intervals after a premature ventricular contraction. An electrophysiological study was performed in all DM1 patients to evaluate ventricular arrhythmias inducibility.

Results. No differences were observed in TS between DM1 and VANH patients (12.3±4.2 and 9.2±3.9 ms/RR, respectively); TO were significantly different between DM1 and VANH (-0.44±2 and -2.9±1.8 % respectively; p 0.02). At electrophysiological study, sustained ventricular arrhythmias were induced in 6 (40%) DM1 patients. We observed a correlation between TO and inducibility of sustained ventricular arrhythmias in DM1 patients: TO -2.29±1.5 in not inducible and 2.32±1.3 % in inducible DM1 patients (p 0.008). No difference between no inducible DM1 (TO -2.28±1.57) and VANH (TO -2.91±1.8 %) was found, while a difference was observed between inducible DM1 and VANH (2.32±4 and -2.9±1.8% respectively; p<0.001).

Conclusions. Our data suggest a dysfunction of the nervous autonomic system, assessed by HRT analysis, in DM1 patients respect to VANH . The difference is more evident in inducible DM1 patients with the most pathological TO values (>0%). Therefore TO seems an useful non invasive risk predictor of sustained ventricular arrhythmias induced at electrophysiological study in DM1 patients.

11:15 a.m.

882-6 Atrial Turbulence Slope, Beta-Blocker Treatment, and Age Identify Postinfarction Patients Who Might Benefit From Prophylactic Treatment With Amiodarone

Dan Wichterle, John Camm, Marek Malik, General University Hospital, Prague, Czech Republic, St. George's Hospital Medical School, London, United Kingdom

Background: A subgroup analysis of EMIAT trial showed that high-risk patients with depressed heart rate variability (HRV) benefit from treatment with amiodarone. In the same population, we investigated whether low-risk patients might also benefit from the treatment.

Methods: All-cause mortality was compared in the placebo and amiodarone arms (n = 1255) in several subgroups of low-risk patients selected according to clinical and Holter-based predictors with previously established dichotomies (age < 65 yrs, first myocardial infarction (MI), left ventricular ejection fraction > 30%, beta-blocker (BB) treatment, absent diabetes mellitus, thrombolysis for index MI, QRS duration <= 100 ms, HRV index > 20, low-frequency HRV spectral power > 130 ms^2, high-frequency HRV spectral power > 30 ms^2, ventricular and atrial turbulence slope (VTS and ATS) > 2.5 ms/RR).

Results: Highly significant benefit from amiodarone treatment with 91% reduction of all-cause mortality was observed in patients who were < 65 yrs of age and who had ATS > 2.5 ms/RR (23% of total population). Normal ATS in younger patients on amiodarone has negative predictive value of 99.3 and 100% for all-cause and arrhythmic mortality, respectively.

Cox regression analysis - association of amiodarone treatment with all-cause mortality reduction

Subgroup	n	relative risk	95% CI	p
Age < 65 yrs	764	0.77	0.49 - 1.21	0.26
BB treatment	559	0.72	0.41 - 1.27	0.25
ATS > 2.5 ms/RR	404	0.46	0.19 - 1.11	0.075
Age < 65 yrs and BB treatment	359	0.34	0.12 - 0.93	0.028
Age < 65 yrs and ATS > 2.5 ms/RR	286	0.09	0.01 - 0.73	0.005
BB treatment and ATS > 2.5 ms/RR	211	0.12	0.02 - 0.94	0.015

Conclusion: Stratification using ATS, BB treatment, and age served to find the low-risk subgroups of postinfarction patients with left ventricular dysfunction who significantly benefit from treatment with amiodarone.

11:30 a.m.

882-7 Abnormal Heart Rate Variability is Significantly Associated With Sudden Cardiac Death Among the Community-Dwelling Elderly

Phyllis K. Stein, Nona Sotooadehnia, Peter P. Domitrovich, David Siscovick, Emily Larsen, John Gottdiener, Pentti Rautaharju, Washington University School of Medicine, St. Louis, MO, University of Washington, Seattle, WA

Background: Associations between decreased heart rate variability (HRV) and risk of sudden cardiac death (SCD) have been found in patient populations. It is not known if HRV is associated with SCD in the community-dwelling elderly.

Methods: Of 1649 subjects with eligible Holter recordings in the Cardiovascular Health Study, N=49 died suddenly during up to 14 yrs of follow up. Time to SCD was 4.7±0.4 (range 0.15-10.4) yrs. They were age/gender matched 2:1 with controls, alive at the time of death of the case, who did not die suddenly on follow up. Subjects were 74±5 yrs, 99M, 47F. Traditional 24-hr time and frequency-domain HRV as well as non-linear indices and ventricular premature complex (VPC) counts were determined and compared between groups via t-tests.

Results: No significant differences were seen between groups in heart rate, or in most time domain HRV indices. Among short-term HRV indices, reflecting beat-by-beat changes, rMSSD and pNN50 tended to be higher (p<0.06) and pNN6.25% (8.8±12.3 vs. 4.7±6.3, p=0.032) was higher for SCD, as was the VPC count (1466 ± 2778 vs. 451±1506, p=0.005). In the frequency domain, also consistent with increased short-term variability, both the LF(low frequency power)/HF(high frequency power) ratio (3.4 ± 2.1 vs. 4.6±2.7, p=0.017) and normalized LF (42 ±9% vs. 47± 9%, p=0.003) were lower, and normalized HF power (18±8% SCD vs. 22±10%, p=0.020) was significantly higher among SCD. Among non-linear HRV indices, which measure the degree of randomness or correlatedness of HR patterns, DFA1 was significantly lower (0.95±0.19 vs. 1.07±0.18, p=0.001) and SD12 was significantly higher (0.32 ±0.16 vs. 0.25 ±0.09) consistent with increased randomness of HR, i.e., increased non-respiratory sinus arrhythmia.

Conclusions: In contrast to clinical population studies, decreased long-term HRV was not associated with SCD among community-based elderly. However, increases in time domain and frequency domain indices reflecting relatively increased short-term HRV, together with non-linear results, are consistent with an increase in beat-to-beat randomness of heart rate patterns among elderly persons at increased risk of sudden death.

11:45 a.m.

882-8 **Prevalence and Clinical Relevance of Short QT Interval in 12,012 Apparenthly Healthy Individuals.**

Giovanni B. Forleo, Lucia De Luca, Luca Santini, Claudia Postorino, Maurizio Aracri, Valeria Morgia, Giulia Magliano, Fabio Di Liberato, Ruggero Mango, Clarissa Cola, Fabrizio Clementi, Roberto Leo, Francesco Romeo, University of Tor Vergata, Rome, Italy

BACKGROUND: Short QT interval (QTI) was recently associated with increased risk of life-threatening arrhythmias and may allow identifying a subset of high-risk patients by ECG observation. To our knowledge no epidemiological short QTI surveys have ever been reported and whether short QTI is associated with clinical events in a non hospital-based population is uncertain. We sought to study prevalence and prognosis of short QTI recognized by chance in subjects without demonstrable structural heart disease.
METHODS: We analyzed ECGs and clinical data of 12,012 apparently healthy European adults undergoing routine medical examinations for occupational reasons. All subjects underwent a medical examination, blood sampling testing and 12-lead ECG. Enrollment was confined to persons without evidence of heart disease or electrolytic imbalance. All subjects ECG records (91% male, age 29.9 ± 10 years) were reviewed by two investigators. QRS duration, QTI and RR interval were measured and predicted QTI (QTp) was calculated by means of QTp formula: 656/(1+Heart Rate/100).
RESULTS: Prevalence of patients with QTI shorter than 80% of predicted value was 0.12% (CI: 0.07-0.21%; 15 of 12,012 subjects), all male (P:NS). In 13 cases (87%), we had clinical information available. No sudden death or significant cardiac arrhythmias were recorded among these patients in a follow-up of 11.56±5.2 years (range 3-18).
CONCLUSIONS: A substantial number of subjects with short QTI were observed in a non hospital-based population. An incidental finding of this ECG pattern in otherwise healthy subjects may have a benign clinical course.

ORAL CONTRIBUTIONS

883 Outcome in Patients Undergoing Biventricular Device Implantation

Wednesday, March 09, 2005, 10:30 a.m.-Noon
Orange County Convention Center, Room 232A

10:30 a.m.

883-3 **Renal Insufficiency: A Potent and Previously Unrecognized Risk for Infection After Device Implantation**

Heather L. Bloom, Brian Heeke, Angel Leon, David Delurgio, Fernando Mera, John Beshai, Jonathan J. Langberg, Emory University, Atlanta, GA

Background: As indications for devices expand, more patients with comorbidities undergo implantation. Medicare data shows increasing rates of infection between 1990 and 1999. The introduction of cardiac resynchronization therapy (CRT) has exposed a sicker patient population to longer procedures, making it likely that infection rates have continued to rise. We reviewed our device experience from 1999 to the present to determine risk factors for infection.
Methods: A case-control study design was used. Of the 4111 device procedures, 65 (1.6%) subsequently underwent lead extraction for infection. An additional 76 patients were referred to us for extraction of infected systems. These 141 patients were compared to 158 consecutive patients whose device implants were not complicated by infection.
Results: Infection was more common in men (77% vs. 61%, p= <.002). Diabetes and warfarin use also increased risk of infection (OR 2.3, 2.8, p<.002,<.001). Neither obesity (BMI>30) or underweight (BMI<18) were associated with infection. The type of procedure (new implant vs replacement) did not predispose to infection. Renal insufficiency (Cr>1.7) was much more common in patients with infection than controls (25.2% vs. 5.8 %, p<.001). Patients with infection were also more likely to be on hemodialysis (6.5% vs. 1.3%, p<.001). Renal insufficiency and hemodialysis were associated with a 5.5 and a 5.4 fold increase in the incidence of infection. The OR for a CrCl<50ml/min was 11.9 (46% vs. 6.6%).
Conclusions: As has been shown in previous studies, diabetes and anticoagulation increase the risk of infection following device implantation or replacement. In the current study, renal insufficiency was the most potent risk factor for infection, with odds ratios more than twice that of any other parameter. Awareness of this previously unrecognized association may facilitate patient selection for device therapy and postoperative management as well.

10:45 a.m.

883-4 **Radiographic LV-RV Inter-Lead Distance Predicts The Hemodynamic Response To Cardiac Resynchronization.**

E. Kevin Heist, Dali Fan, Daniel Arzola-Castaner, Theofanie Mela, Michael H. Picard, Vivek Y. Reddy, Moussa Mansour, Jeremy N. Ruskin, Jagmeet P. Singh, Massachusetts General Hospital, Boston, MA

Background: Maximal separation between right and left ventricular leads is commonly sought during cardiac resynchronization therapy (CRT), but there is little data to support this practice. This study examines the relationship between relative LV and RV lead position and effects of CRT on contractility.
Methods: 101 consecutive patients undergoing CRT for standard indications were screened for this single center study. Of these, 51 (age 69±10 y, LVEF 20±8) with transvenous LV lead placement and sufficient mitral regurgitation for non-invasive hemodynamic analysis were included. Echocardiographic assessment of contractility was measured by Doppler analysis of mitral regurgitation as a percentage change in dP/dt (dP/dt) with CRT on and off. The horizontal and vertical coordinates of the LV and RV leads was determined on post-procedural PA and lateral radiographs, with correction for the cardio-thoracic ratio.
Results: The corrected LV to RV inter-lead distance on the lateral radiograph (15.8±3.9 cm) correlates well with dP/dt (36.5±47.1%) (n=51, r=0.43, p=0.002). Further analyses show that the inter-lead distance in the horizontal plane (r=0.58, p<0.0001) and not the vertical plane (r=-0.28, p=NS) is associated with dP/dt. A significant correlation between the horizontal inter-lead distance on the lateral film and dP/dt was observed only in subjects with ischemic cardiomyopathy (n=34, r=0.69, p<0.0001), and not those with non-ischemic cardiomyopathy (n=17, r=0.21, p=NS). In the ischemic subgroup, the corrected horizontal inter-lead distance is greater in acute responders (dP/dt>25%) (n= 15; 16.8±3.3 cm) compared to non-responders (n= 19; 9.5±6.2 cm) (p=0.0002). Other radiographic measures, including the inter-lead distance (direct as well as horizontal and vertical components) on the PA film and the distance of the LV lead tip from base to apex did not correlate with dP/dt.
Conclusion: The horizontal LV to RV inter-lead distance on the lateral chest radiograph is a useful predictor of the acute hemodynamic response to CRT in patients with ischemic cardiomyopathy. Use of these findings with a lateral fluoroscopic view during lead placement may improve the benefit derived from CRT.

11:00 a.m.

883-5 **Left Ventricular Remodeling after Cardiac Resynchronization Therapy Reduces Inducibility of Ventricular Tachy-Arrhythmias**

Philippine Kiès, Jeroen J. Bax, Sander G. Molhoek, Gabe B. Bleeker, Katja Zeppenfeld, Marianne Bootsma, Lieselot van Erven, Paul Steendijk, Ernst E. van der Wall, Martin J. Schalij, Leiden University Medical Center, Leiden, The Netherlands

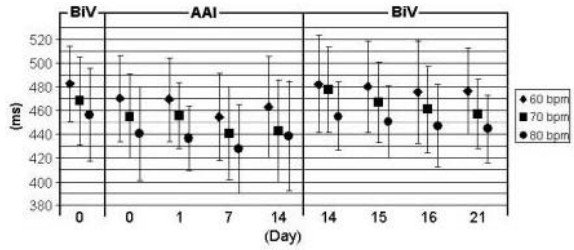
Introduction: Severe heart failure patients are at high risk of cardiac death due to ventricular arrhythmias or progressive heart failure. Therefore these patients may benefit from implantable cardioverter defibrillator (ICD) therapy and/or cardiac resynchronization therapy (CRT). Several reports have suggested that CRT may decrease the frequency of ventricular arrhythmias. We evaluated by electrophysiological study the effect of CRT on the inducibility of ventricular arrhythmias in relation to reverse remodeling after 6 months of CRT.
Methods: Eighteen patients (15 men, mean age 62±11 yrs), eligible for treatment with a combined CRT-ICD device, have been evaluated by electrophysiological study before implantation of the device and after 6 months of therapy. In addition left ventricular (LV) end-diastolic (EDV) and end-systolic volumes (ESV) were echocardiographically measured before and after 6 months of CRT.
Results: Before CRT, in 15 (83%) patients a sustained ventricular tachycardia was inducible during electrophysiological study. After 6 months of CRT, in only 6 (33%) patients a sustained ventricular tachycardia was inducible (P<0.01). None of the patients showed increased inducibility. Anti-arrhythmic drug usage did not differ between both electrophysiological studies. The patients who showed loss of inducibility showed significant reverse remodeling (LVEDV from 293±67 to 258±69 ml and LVESV from 244±69 to198±69 ml, both p<0.01) as opposed to the patients who remained inducible (LVEDV from 258±30 to 252±41; LVESV from 208±27 to 199±35 ml, both ns).
Conclusion: In patients with severe heart failure, six months of CRT resulted in a significant reduction of inducible ventricular arrhythmias, in patients showing significant reverse remodeling as a result of CRT.

11:15 a.m.

883-6 **Pro-arrhythmic State Following the Initiation of Cardiac Resynchronization Therapy in Patients With Heart Failure**

Frieder Braunschweig, Hannes Pfizenmayer, Aigars Rubulis, Cecilia Linde, Lennart Bergfeldt, Karolinska University Hospital, Stockholm, Sweden

Cardiac Resynchronisation Therapy (CRT) is increasingly used in patients with heart failure. Occasionally, ventricular arrhythmia and sudden cardiac death has been reported in association with the initiation of biventricular stimulation (BiV).
Methods: In 15 pts (61±12 yr, EF 22±8 %, QRS 168±25 ms), BiV was suspended for 14 d by programming the pacemaker to atrial-inhibited mode (AAI). The QT interval was assessed on 9 occasions: day 0 (BiV); day 0, 1, 7, and 14 (AAI); day 14, 15, 16, and 21 (BiV). Twelve-lead ECG recordings were obtained at 50 mm/s with the pacemaker programmed to 60, 70 and 80 bpm, all preceded by 5 min of supine rest. The QT interval, average of 3 cycles, was assessed as the mean of all measurable leads.
Results: BiV was associated with a significant QT prolongation (p<0.05). Immediately after re-initiation of BiV (day 14), the QT interval increased on average by 5% (p<0.01). The figure shows a significant rate dependence (p<0.01), and suggests a time dependent shortening of the QT interval after BiV reactivation. Conclusion: BiV was associated with a significant prolongation of the QT-interval, suggesting the induction of a pro-arrhythmic state. This is in agreement with occasional reports on malignant arrhythmia and sudden cardiac death occuring in close relation to the initiation of CRT. Pacing at higher heart rates resulted in a shortened repolarization and may be considered for arrhythmia prevention, at least during the initial phase of CRT.



11:30 a.m.

883-7

Improvements in Left Ventricular Diastolic Function After Cardiac Resynchronization Therapy: Results at Four-Month and 12-Month Follow-up

Alan D. Waggoner, Mitchell N. Faddis, Lisa de las Fuentes, Marye J. Gleva, Sharon Heuerman, Victor G. Davila-Roman, Washinton University, St. Louis, MO

Introduction: Cardiac resynchronization therapy (CRT) decreases left ventricular (LV) volumes and increases ejection fraction (EF) in patients with heart failure. The CRT-related improvements in LV diastolic function have not been evaluated by relative load-independent, non-invasive measurements.

Methods: 34 patients (age 61±10 years, 65% male, 26% ischemic etiology) were studied with two-dimensional and pulsed-wave Doppler (PWD) echocardiography, tissue Doppler imaging (TDI) and color M-Mode flow propagation (FP), prior to CRT, 4±2 months (mo), and 12±2 mo after CRT. Measurements included LV volumes, LVEF, PWD mitral E/A ratio, deceleration time (DT), diastolic filling time (DFT) and isovolumic relaxation time (IVRT). TDI early diastolic (Em at septal annulus) and FP velocities were obtained in apical 4 chamber view; PWD mitral E wave/FP was used to estimate LV filling pressure.

Results:

	EDV (ml)	ESV (ml)	LVEF (%)	E/A	DT (ms)	DFT (ms)	E/FP
Pre CRT	233±90	176±78	26±5	1.5±1.1	181±46	351±84	2.2±0.6
4 mo	194±81	132±74	35±11	1.2±0.9	209±60	446±126	1.8±0.7
12 mo	190±82	131±77	35±13	1.2±0.7	232±79	447±110	1.9±0.8
ANOVA	.07	.02	.0003	.29	.005	.0003	.06
Mean ± SD; ANOVA with post-hoc analysis by Fisher's least-significant-difference.							

After 4 mo of CRT, end-systolic volume (ESV) decreased, LVEF and DFT both increased, but without further interval changes at 12 mo. LV filling pressures (E/FP) also decrease at 4 mo (p=.03). DT increased significantly at 12 mo after CRT. The mitral E/A ratio and LV relaxation indices (IVRT, Em, and FP) were unchanged after CRT.

Conclusions: CRT improves LV diastolic filling in patients with severe heart failure and modestly decreases filling pressure. The findings are associated with reduction in LV volumes and improvement in LVEF. The benefits of CRT observed at short term follow-up are sustained at 1 year.

11:45 a.m.

883-8

Gender-related Long-Term Outcome in Heart Failure Patients Treated With Cardiac Resynchronisation Therapy

Cecilia Fantoni, Santi Raffa, Francois Regoli, Mihoko Kawabata, Helmut U Klein, Angelo Auricchio, University Hospital, Magdeburg, Germany, University of Insubria, Varese, Italy

Background: Gender-related difference in long-term outcome after CRT has not been investigated so far.

Methods: We compared improvement of functional capacity and echo-parameters at 1 year follow-up and long term event free survival rate in 139 male and 35 female heart failure patients consecutively implanted with a CRT device, using a transvenous lead. Events considered for survival rate analysis were death for any cause, heart transplantation and left ventricular (LV) assist device implantation.

Results: At baseline men were younger than women (62±9 vs 66±7 yrs, p<0,04). Mean capillary wedge pressure was higher in male (16,2±9,8 vs 11,9±7,7 mmHg, p<0,03). All the other clinical, echocardiographic and hemodynamic variables were not different between the 2 groups. Rate of a defibrillator back-up was higher in male (p<0,02). At 1 year follow-up NYHA class, LV ejection fraction, LV diameters, mitral regurgitation and peak oxygen consumption significantly improved in both groups compared to baseline. During a mean follow-up of 683±444 days 20 events occurred among men (14%) and only 1 among women (3%). Male patients demonstrated a significant worse outcome after CRT compared to female as shown by the Kaplan-Meyer event-free survival curves (p<0,05).

Conclusions: Male patients show a significant worse outcome after CRT compared to female, in spite of similar baseline clinical profile and equal functional improvement at 1 year follow-up. These results need to be confirmed by prospective randomised trials.